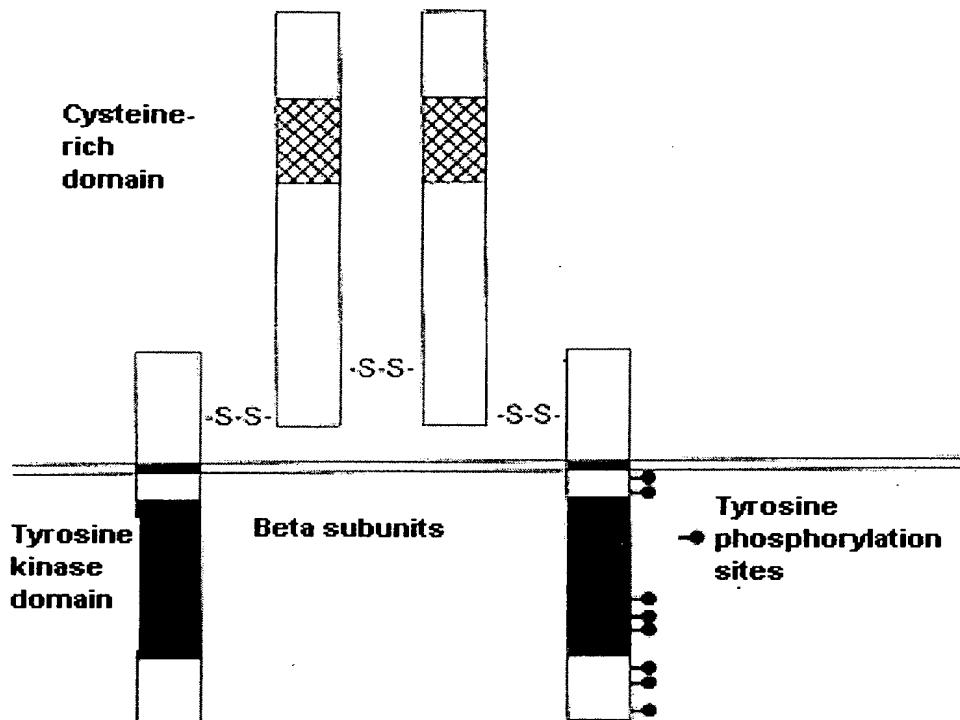




**Alpha subunits**



**FIGURE 1**

BEST AVAILABLE COPY

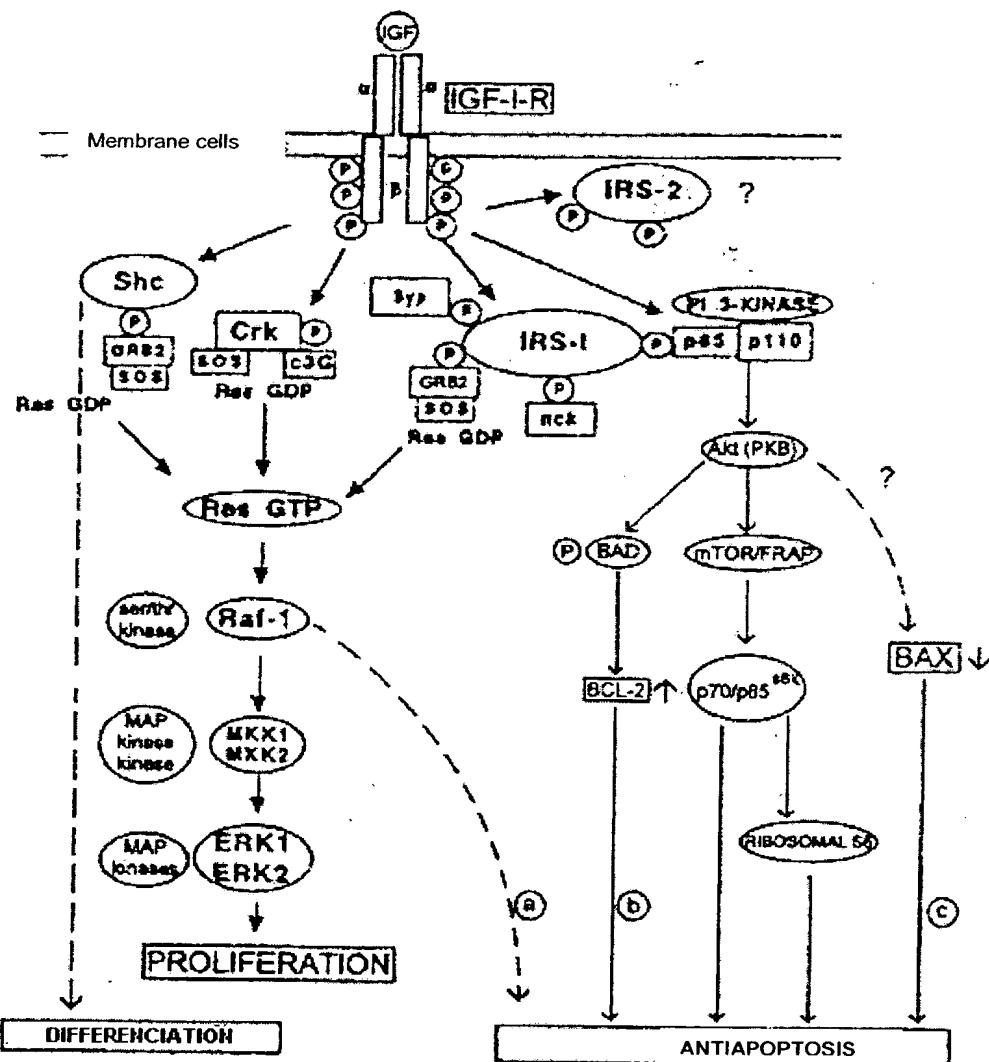
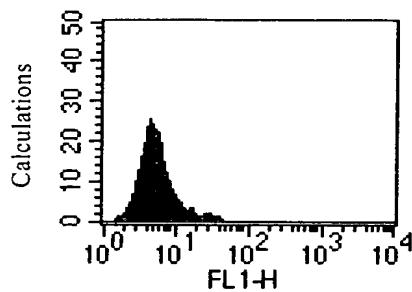
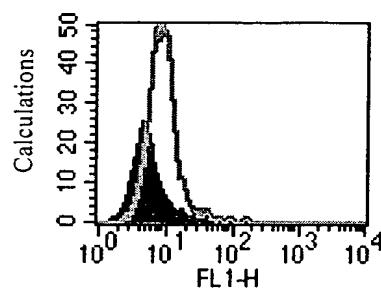


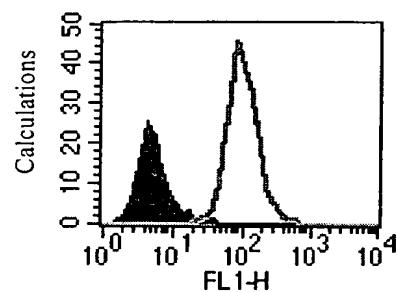
FIGURE 2



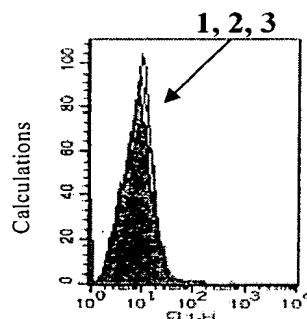
**FIGURE 3A**



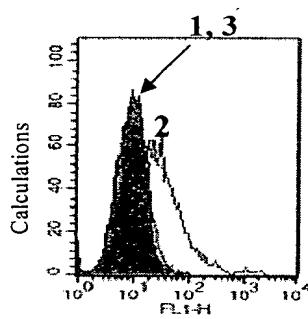
**FIGURE 3B**



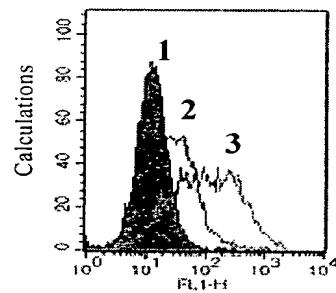
**FIGURE 3C**



**Nontransfected cells**



**IGF-IR+ cells**



**IR+ cells**

**FIGURE 4A**

**FIGURE 4B**

**FIGURE 4C**

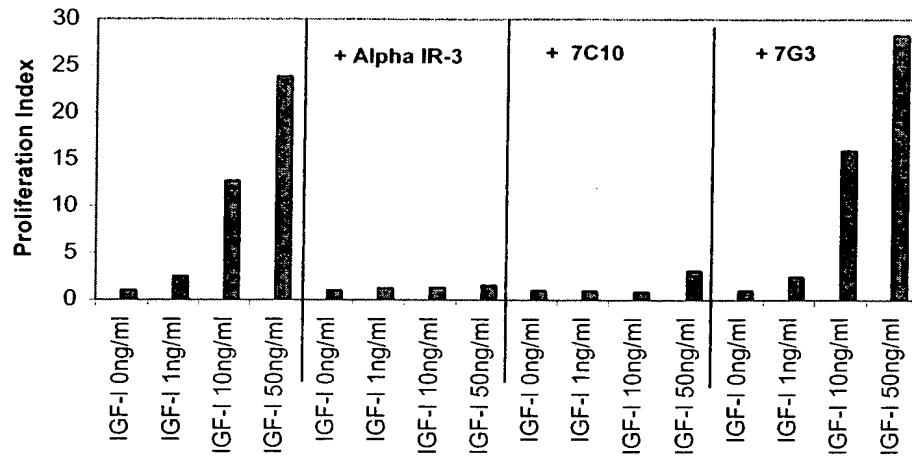


FIGURE 5

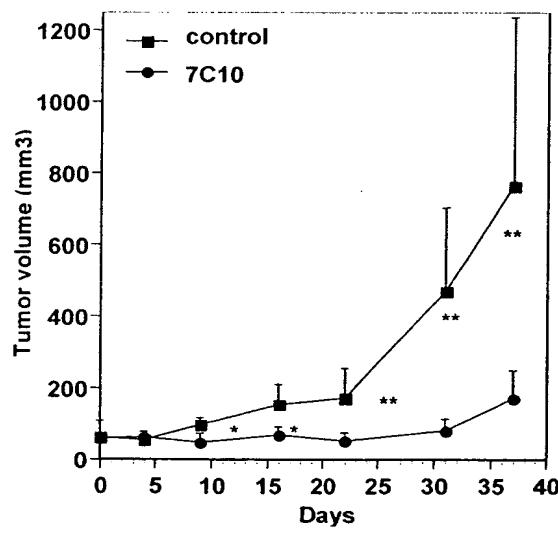


FIGURE 6A

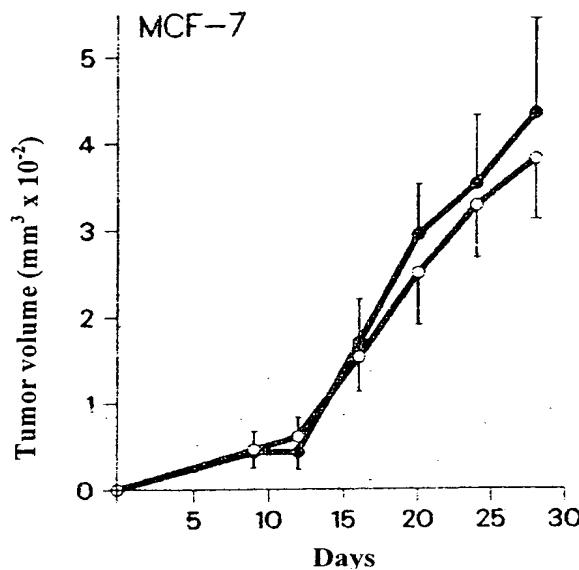


FIGURE 6B

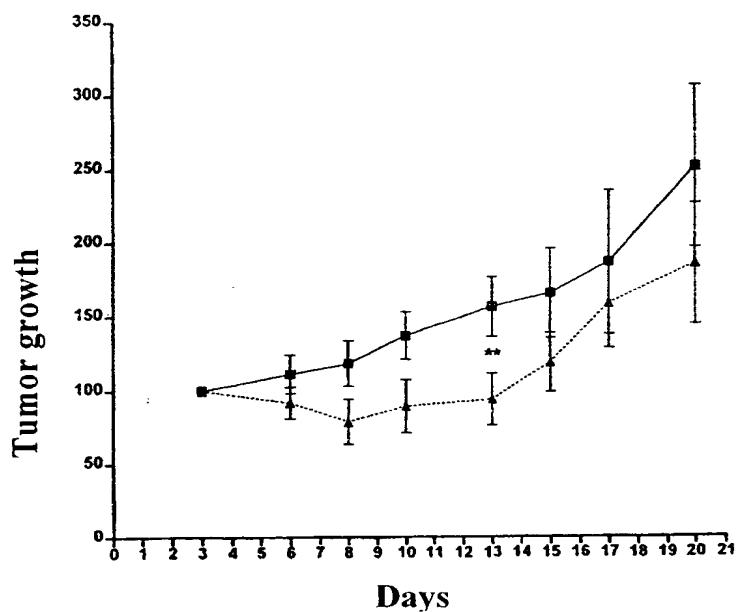


FIGURE 6C

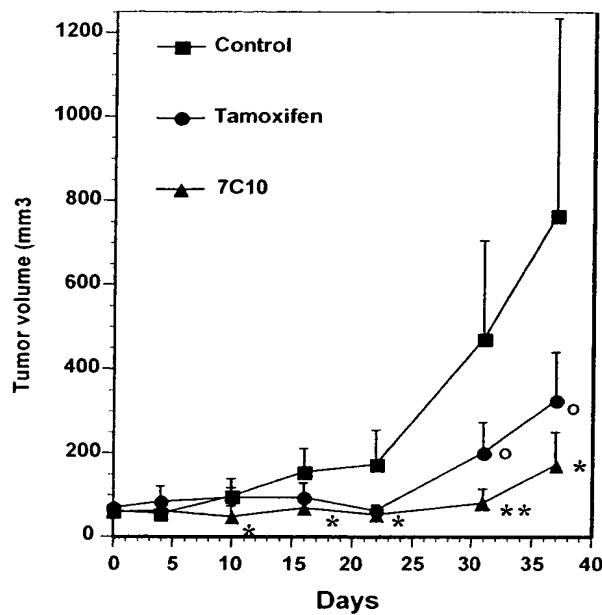


FIGURE 7

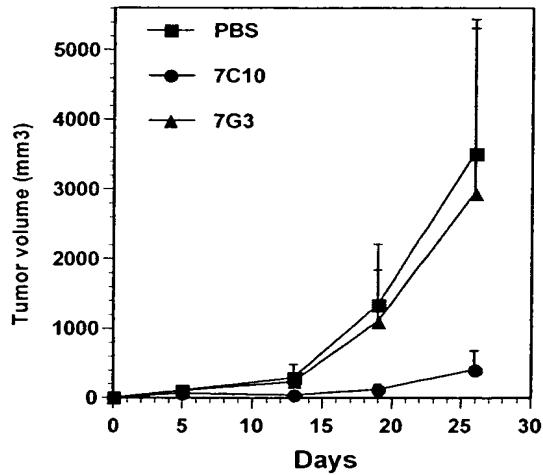


FIGURE 8A

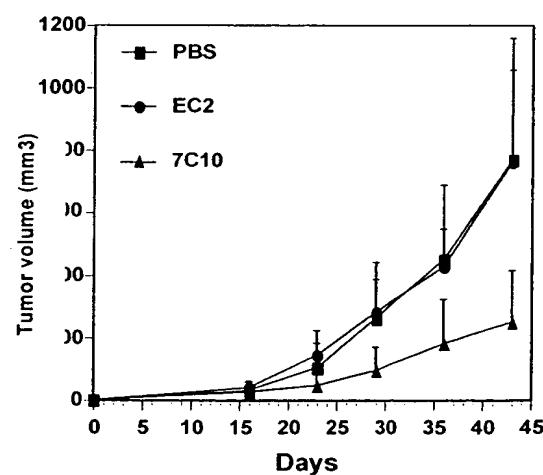


FIGURE 8B

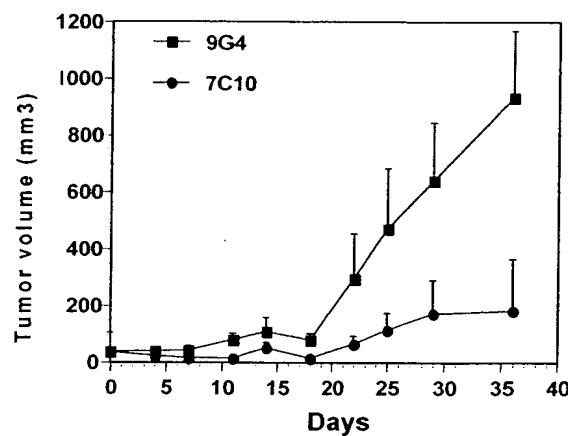


FIGURE 8C

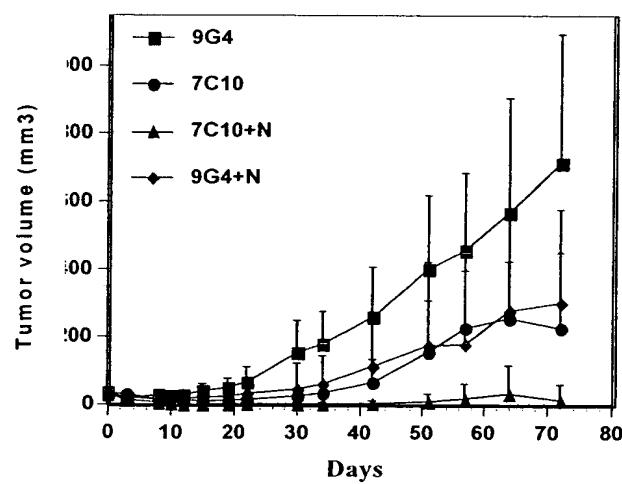


FIGURE 9

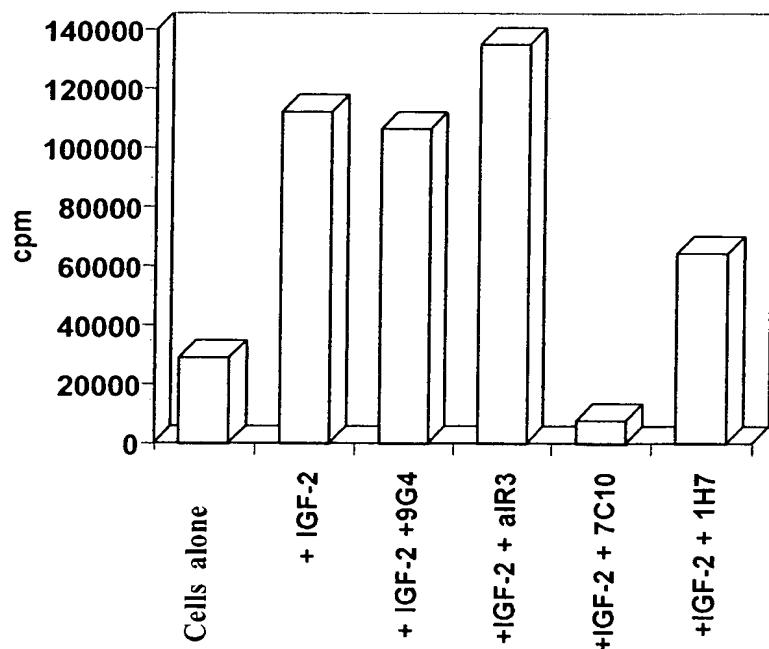


FIGURE 10

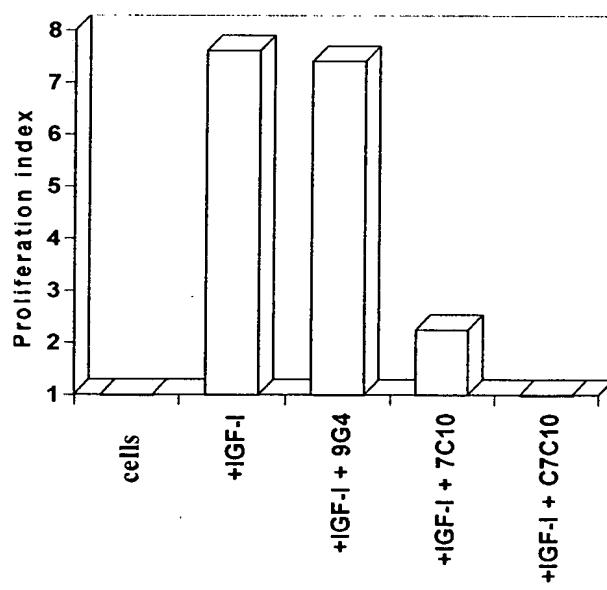


FIGURE 11

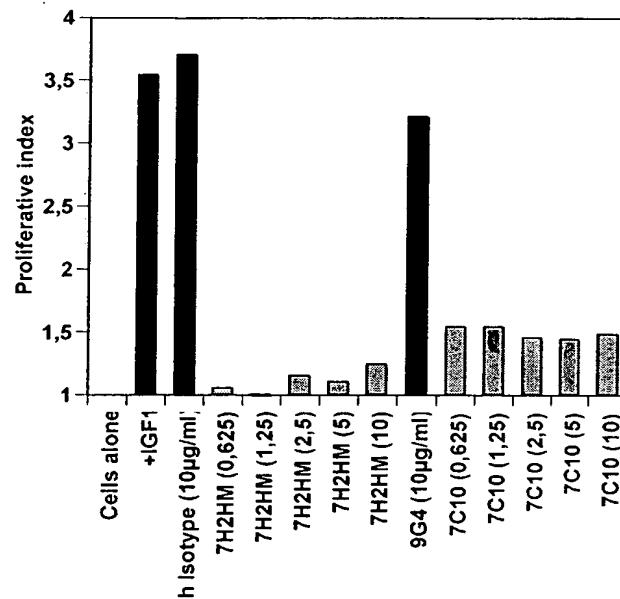


FIGURE 12

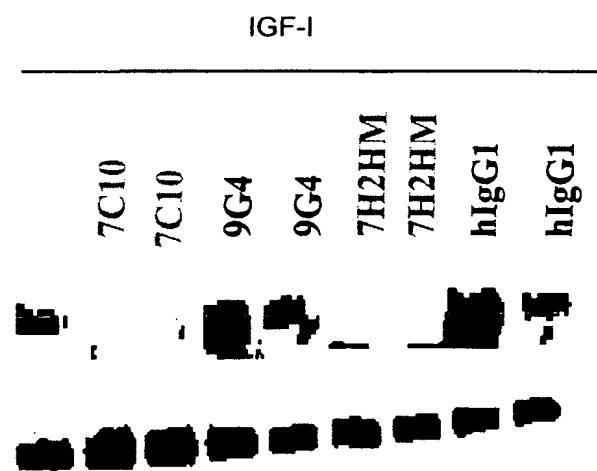


FIGURE 13

ATGAAGTTGCCTGTTAGGCTGTTGGTGTGATGTTCTGGATTCCTGCTTCCAGAAGTGAT  
 1 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 60  
 TACTTCAACGGACAATCCGACAACCACGACTACAAGACCTAAGGACGAAGGTCTCACTA  
**ATGAAGTTGCCTGTTAGGCTGTTGGTGTGATGTTCTGGTGTGCTGCTTCCAGAAGTGAT**  
 oligo MKV-1            L M F W I P A S R S D -  
 3' end                 leader peptide  
 GTTTTGATGACCCAAATTCCACTCTCCCTGCCTGTCAGTCTTGGAGATCAAGCCTCCATC  
 61 -----+-----+-----+-----+-----+-----+-----+-----+ 120  
 CAAAACACTGGGTTAACGGTGAGAGGGACGGACAGTCAGAACCTCTAGTTCGGAGGTAG  
 V L M T Q I P L S L P V S L G D Q A S I -  
 TCTTGCAGATCTAGTCAGAGCATTGTACATAGTAATGGAAACACCTATTACAATGGTAC  
 121 -----+-----+-----+-----+-----+-----+-----+-----+ 180  
 AGAACGTCTAGATCAGTCTCGTAACATGTATCATTACCTTGTGGATAATGTTACCATG  
 S C R S S Q S I V H S N G N T Y L Q W Y -  
 CDR 1  
 CTGCAGAAACCAGGTCAGTCTCAAAGCTCCTGATCTACAAAGTTCCAACCGACTTTAT  
 181 -----+-----+-----+-----+-----+-----+-----+-----+ 240  
 GACGTCTTGGTCCAGTCAGAGGTTTCGAGGACTAGATGTTCAAAGGTGGCTGAAATA  
 L Q K P G Q S P K L L I Y K V S N R L Y -  
 CDR 2  
 GGGGTCCCAGACAGGTTCAGTGGCAGTGGATCAGGGACAGATTCACACTCAAGATCAGC  
 241 -----+-----+-----+-----+-----+-----+-----+-----+ 300  
 CCCCAGGGTCTGTCCAAGTCACCGTCACCTAGTCCCTGTCTAAAGTGTGAGTTCTAGTCG  
 G V P D R F S G S G S G T D F T L K I S -  
 AGCGTGGAGGCTGAGGATCTGGGAGTTATTACTGCTTCAAGGTTCACATGTTCCGTGG  
 301 -----+-----+-----+-----+-----+-----+-----+-----+ 360  
 TCGCACCTCCGACTCCTAGACCCCTAAATAATGACGAAAGTCCAAGTGTACAAGGCACC  
 S V E A E D L G V Y Y C F Q G S H V P W -  
 CDR 3  
 GG  
 ACGTTCGGTGGAGGCCACCAAGCTGGAAATCAAACGGGCTGATGCTGCACCAACTGTATCC  
 361 -----+-----+-----+-----+-----+-----+-----+-----+ 420  
 TGCAAGCCACCTCCGTGGTTCGACCTTAGTTGCCCGACTACGACGTGGTGTGACATAGG  
 T F G G G T K L E I K  
 MKC oligo  
**TAGAAGGGTGGTAGGTCA**  
 ATCTTCCCACCATCCAGT  
 421 -----+----- 438  
**TAGAAGGGTGGTAGGTCA**

**FIGURE 14**

ATGATGGTGTAAAGTCTCTGTACCTCTTGACAGCCATTCTGGTATCCTGTCTGATGTA  
 1 -----+-----+-----+-----+-----+-----+ 60  
 TACTACCACAATTCAAGAACATGGACAACTGTCGGTAAGGACCATAGGACAGACTACAT  
**MHV-12** **ATGATGGTGTAAAGTCTCTGTACCT**  
**MHV-8** **ATGAGAGTGCTGATTCTTTGTG**

L	L	T	A	I	P	G	I	L	S	D	V	-
<i>3' end leader peptide</i>												

CAGCTTCAGGAGTCAGGACCTGGCCTCGTAAACCTTCTCAGTCTCTGTCTCACCTGC  
 61 -----+-----+-----+-----+-----+-----+ 120  
 GTCGAAGTCCTCAGTCCTGGACCGGAGCATTGGAAGAGTCAGAGACAGAGAGTGGACG

Q   L   Q   E   S   G   P   G   L   V   K   P   S   Q   S   L   S   L   T   C   -

TCTGTCACCGGCTACTCCATACCGGTGGTTATTATGGAACGGATCCGGCAGTTCCA  
 121 -----+-----+-----+-----+-----+-----+ 180  
 AGACAGTGGCCGATGAGGTAGTGGCCACCAATAAACCTTGACCTAGGCCGTCAAAGGT

S   V   T   G   Y   S   I   T   G   G   Y   L   W   N   W   I   R   Q   F   P   -  
 CDR 1

GGAAACAAAAGTGGAGTGGATGGGCTACATAAGCTACGACGGTACCAAACTACAAACCA  
 181 -----+-----+-----+-----+-----+-----+ 240  
 CCTTTGTTGACCTCACCTACCCGATGTATTGCTGCCATGGTTATTGATGTTGGT

G   N   K   L   E   W   M   G   Y   I   S   Y   D   G   T   N   N   Y   K   P   -  
 CDR 2

TCTCTCAAAGATCGAATCTCCATCACTCGTGACACATCTAAGAACAGTTTCCTGAAG  
 241 -----+-----+-----+-----+-----+-----+ 300  
 AGAGAGTTCTAGCTTAGAGGTAGTGAGCACTGTGTAGATTCTGGTCAAAAGGACTTC

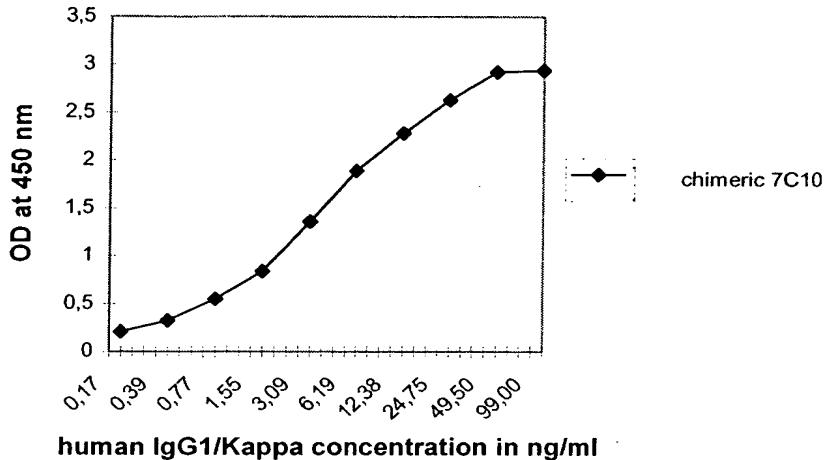
S   L   K   D   R   I   S   I   T   R   D   T   S   K   N   Q   F   F   L   K   -  
 TTGAATTCTGTGACTAATGAAGACACAGCTACATATTACTGTGCAAGATACGGTAGGGTC  
 301 -----+-----+-----+-----+-----+-----+ 360  
 AACTTAAGACACTGATTACTCTGTGTCGATGTATAATGACACGTTATGCCATCCCAG

L   N   S   V   T   N   E   D   T   A   T   Y   Y   C   A   R   Y   G   R   V   -  
 CDR 3  
**GGG**

TTCTTTGACTACTGGGCCAAGGCACCACTCTCACAGTCTCCTCAGCCAAAACGACACCC  
 361 -----+-----+-----+-----+-----+-----+ 420  
 AAGAAACTGATGACCCCGGTTCCGTGGTGAGAGTGTCAAGAGGAGTCGGTTTGCTGTGGG

F   F   D   Y   W   G   Q   G   T   T   L   T   V   S   S  
**oligo MHC-1**  
**GGTAGACAGATAGGTGAC**  
**CCATCTGTCTATCCACTG**  
 421 -----+----- 438  
**GGTAGACAGATAGGTGAC**

**FIGURE 15**



**FIGURE 16**

**CDR 1**

7C10 VL mouse	DVLMTQ <u>I</u> PLSLPVSLGDQASISC	<b>RSSQSIVHSNGNTYLO</b>
DRB1-4 .3	.....T.....	..... <b>E</b>
C94-5B11' CL	.....T.....	..... <b>E</b>
Kabat sgII mouse	V... <u>T</u> .....	..... <b>L</b> ..... <b>E</b>

**CDR 2**

7C10 VL mouse	WYLQKPGQSPKLLIY	<b>KVSNRLY</b> GVPDRFSGSGSGTDFTL
DRB1-4 .3	.....	..... <b>FS</b> .....
C94-5B11' CL	.....	..... <b>FS</b> .....
Kabat sgII mouse	.....	..... <b>FS</b> .....

**CDR 3**

7C10 VL mouse	KISSVEAEDLGVYYC	<b>FQGSHVPWT</b> FGGGTKLEIK
DRB1-4 .3	...R.....	..... <b>F</b> ..S....D..
C94-5B11' CL	...R.....	.....
Kabat sgII mouse	... <u>R</u> .....	..... <b>T</b> ... <b>Y</b> .....

**FIGURE 17**

**CDR 1**

7C10 VL mouse	DVLMTQIPLSLPVSLGDQASISC	<u>RSSQSIVHSNGNTYLO</u>
GM607	.IV...S.....TP.EP.....	LL....YN..D
DPK15/A19	.IV...S.....TP.EP.....	LL....YN..D
Kabat sgII hu	.IV...S.....TP.EP.....	LL..D.XX..X

**CDR 2**

7C10 VL mouse	WYLQKPGQSPKLLIY	<u>KVSNRLY</u>	GVPDRFSGSGSGTDFTLK
GM607	.....Q....	LG...AS	.....
DPK15/A19	.....Q....	LG...AS	.....
Kabat sgII hu	.....Q....	L...AS	.....

**CDR 3**

7C10 VL mouse	ISSVEAEDLGVYYC	<u>FQGSHVPWT</u>	FGGGTKLEIK
GM607	..R.....V.....	M.ALQT.Q.	..Q...V...
DPK15/A19	..R.....V.....	M.ALQT.	
Kabat sgII hu	..R.....V.....	M.ALQX.R.	..Q...V...

**FIGURE 18**

**CDR 1**

7C10 VL mouse	DVLMTQIPLSLPVSLGDQASISC	<u>RSSQSIVHSNGNTYLO</u>
GM 607	.IV...S.....TP.EP.....	LL....YN..D
7C10 VL Humanized 1	.V...S.....TP.EP.....	.....
7C10 VL Humanized 2	.IV...S.....TP.EP.....	.....

**CDR 2**

7C10 VL mouse	WYLQKPGQSPKLLIY	<u>KVSNRLY</u>	GVPDRFSGSGSGTDFTL
GM 607	.....Q....	LG...AS	.....
7C10 VL Humanized 1	.....Q....	.....	.....
7C10 VL Humanized 2	.....Q....	.....	.....

**CDR 3**

7C10 VL mouse	KISSVEAEDLGVYYC	<u>FQGSHVPWT</u>	FGGGTKLEIK
GM 607	...R.....V.....	M.ALQT.Q.	..Q...V...
7C10 VL Humanized 1	...R.....V.....	.....	..Q...V...
7C10 VL Humanized 2	...R.....V.....	.....	..Q...V...

**FIGURE 19**

MluI

GTCAGAACGCGTGCCGCCACCATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGG  
 1 -----+-----+-----+-----+-----+-----+-----+ 60  
 CAGTCTGCGCACGGCGGTGGTACTTCAACGGACAATCCGACAACCACGACTACAAGACC

M	K	L	P	V	R	L	L	V	L	M	F	W	-
---	---	---	---	---	---	---	---	---	---	---	---	---	---

Peptide leader

TTTCCTGCTTCCAGCAGTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACC  
 61 -----+-----+-----+-----+-----+-----+-----+ 120  
 AAAGGACGAAGGTCGTCACTACAAACACTACTGAGTCAGAGGTGAGAGGGACGGCAGTGG

2

F	P	A	S	S	S	D	<u>V</u>	V	M	T	Q	S	P	L	S	L	P	V	T	-
---	---	---	---	---	---	---	----------	---	---	---	---	---	---	---	---	---	---	---	---	---

CCTGGAGAGCCGGCCTCCATCTCCTGCAGGTCTAGTCAGAGCATTGTACATAGTAATGGA  
 121 -----+-----+-----+-----+-----+-----+-----+ 180  
 GGACCTCTGGCCGGAGGTAGAGGACGTCCAGATCAGTCTCGTAACATGTATCATTACCT

CDR 1

P	G	E	P	A	S	I	S	C	<u>R</u>	S	S	Q	S	I	V	H	S	N	G	-
---	---	---	---	---	---	---	---	---	----------	---	---	---	---	---	---	---	---	---	---	---

KpnI

AACACCTATTGCAATGGTACCTGCAGAACGCCAGGGCAGTCTCCACAGCTCCTGATCTAT  
 181 -----+-----+-----+-----+-----+-----+-----+ 240  
 TTGTGGATAAACGTTACCATGGACGTCTCGGTCCCGTCAGAGGTGTCGAGGACTAGATA

N   T   Y   L   Q   W   Y   L   Q   K   P   G   Q   S   P   Q   L   L   I   Y   -

AAAGTTTCTAATCGGCTTATGGGGTCCCTGACAGGTTCAAGTGGCAGTGGATCAGGCACA  
 241 -----+-----+-----+-----+-----+-----+-----+ 300  
 TTTCAAAGATTAGCCGAAATACCCAGGGACTGTCCAAGTCACCGTCACCTAGTCCGTGT

CDR 2

K	V	S	N	R	L	<u>Y</u>	G	V	P	D	R	F	S	G	S	G	S	G	T	-
---	---	---	---	---	---	----------	---	---	---	---	---	---	---	---	---	---	---	---	---	---

GATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTTGGGTTATTACTGCTTT  
 301 -----+-----+-----+-----+-----+-----+-----+ 360  
 CTAAAATGTGACTTTAGTCGTCTACCTCCGACTCCTACAACCCCAAATAATGACGAAA

D   F   T   L   K   I   S   R   V   E   A   E   D   V   G   V   Y   Y   C   F   -

CAAGGTTCACATGTTCCGTGGACGTTGGCCAAGGGACCAAGGTGGAAATCAAACGTGAG  
 361 -----+-----+-----+-----+-----+-----+-----+ 420  
 GTTCCAAGTGTACAAGGCACCTGCAAGCCGGTCCCTGGTCCACCTTAGTTGCACTC

CDR 3

Q	G	S	H	V	P	<u>W</u>	T	F	G	Q	G	T	K	V	E	I	K	-
---	---	---	---	---	---	----------	---	---	---	---	---	---	---	---	---	---	---	---

BamHI

|  
 TGGAATCCTCTGCG  
 421 -----+--- 433  
 ACCTAGGAGACGC

**FIGURE 20**

MluI

1 GTCAGAACGCGTGCCGCCACCATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGG  
 1 CAGTCTGCGCACGGCGGTGGTACTTCAACGGACAATCCGACAACCACGACTACAAGACC 60

M	K	L	P	V	R	L	L	V	L	M	F	W	-
---	---	---	---	---	---	---	---	---	---	---	---	---	---

Leader peptide

61 TTTCCTGTTCCAGCAGTGATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACC  
 61 AAAGGACGAAGGTCTGTCACTACAACACTACTGAGTCAGAGGTGAGAGGGACGGGCAGTGG 120

F	P	A	S	S	S	D	<u>I</u>	V	M	T	Q	S	P	L	S	L	P	V	T	-
---	---	---	---	---	---	---	----------	---	---	---	---	---	---	---	---	---	---	---	---	---

121 CCTGGAGAGCCGGCCTCCATCTCCTGCAGGTCTAGTCAGAGCATTGTACATAGTAATGGA  
 121 GGACCTCTGGCCGGAGGTAGAGGACGTCCAGATCAGTCTCGTAACATGTATCATTACCT 180

CDR 1

P	G	E	P	A	S	I	S	C	<u>R</u>	S	S	Q	S	<u>I</u>	V	H	S	N	G	-
---	---	---	---	---	---	---	---	---	----------	---	---	---	---	----------	---	---	---	---	---	---

KpnI

181 AACACCTATTGCAATGGTACCTGCAGAACGCCAGGGCAGTCTCCACAGCTCCTGATCTAT  
 181 TTGGATAAACGTTACCATGGACGTCTCGGTCCCGTCAGAGGTGTCGAGGACTAGATA 240

N	T	Y	L	Q	W	Y	L	Q	K	P	G	Q	S	P	Q	L	L	I	Y	-
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---

241 AAAGTTCTAATCGGTTATGGGGTCCCTGACAGGTTCAAGTGGCAGTGGATCAGGCACA  
 241 TTTCAAAGATTAGCCGAAATACCCCAGGGACTGTCCAAGTCACCGTCACCTAGTCGTGT 300

CDR 2

K	V	S	N	R	<u>L</u>	<u>Y</u>	G	V	P	D	R	F	S	G	S	G	S	G	T	-
---	---	---	---	---	----------	----------	---	---	---	---	---	---	---	---	---	---	---	---	---	---

301 GATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTTGGGTTATTACTGCTTT  
 301 CTAAAATGTGACTTTAGTCGTCTCACCTCCGACTCCTACAACCCCAAATAATGACGAAA 360

D	F	T	L	K	<u>I</u>	S	R	V	E	A	E	D	V	G	V	Y	Y	C	<u>F</u>	-
---	---	---	---	---	----------	---	---	---	---	---	---	---	---	---	---	---	---	---	----------	---

361 CAAGGTTCACATGTTCCGTGGACGTTCCGCCAACGGACCAAGGTGGAAATCAAACGTGAG  
 361 GTTCCAAGTGTACAAGGCACCTGCAAGCCGGTCCCTGGTCCACCTTAGTTGCACTC 420

CDR 3'

<u>Q</u>	G	S	H	V	P	<u>W</u>	<u>T</u>	F	G	Q	G	T	K	V	E	I	K	-
----------	---	---	---	---	---	----------	----------	---	---	---	---	---	---	---	---	---	---	---

BamHI

421 TGGATCCTCTGCG  
 421 ACCTAGGAGACGC 433

**FIGURE 21**

17                    27                    **CDR 1**

<b>7C10 VH</b>	<u>DVQLQESGPGLVKPSQSLSLTCSVTGYSIT</u>	<b>GGYLWN</b>	WIRQ
<b>AN03' CL</b>	.....	<b>S..Y..</b>	....
Kabat sgI(A)	E.....S.....T.....D...	<b>S..WN.</b>	....

**CDR 2**

<b>7C10 VH</b>	FPGNKLEWMG	<b>YISYDGTNKYKPSLKD</b>	RISITRDTSKNQFFL
<b>AN03' CL</b>	.....	<b>N...N...N...N</b>	.....
Kabat sgI(A)	.....	<b>S.STY.N...S</b>	..... <u>Y..</u>

84                    **CDR 3**

<b>7C10 VH</b>	<u>KLNSVTNEDTATYYCAR</u>	<b>YGRV-FFDY</b>	WGQGTTLT	VSS
<b>AN03' CL</b>	.....T.....	<b>E.YGY..</b>	.....	.....
Kabat sgI(A)	<u>Q.....T.....</u>	<b>G.YGYG..</b>	.....	<u>V....</u>

**FIGURE 22**

	<b>Rch 1</b>	30 <b>CDR 1 Rch 2</b>
7C10 VH mouse	DVQLQESGPGLVKPSQSLSLTCS <u>VTGYSIT</u>	<b>GGYLWN</b> WIRQ
human Kabat sgII	Q.....T.....T.S. <u>G.VS</u>	<b>SYWS..</b> ....
human VH FUR1'CL	Q.....ET.....T.S....S	<b>S..Y.S</b> ....
human Germline	Q.....ET.....T.S....S	<b>S..Y.S</b> ....

	<b>Rch 2</b>	48 <b>CDR 2</b>	67    71 <b>Rch 3</b>
7C10 VH mouse	FPGNKLEWMG	<b>YISYDGTNKYKPSLKD</b>	RISIT <u>R</u> DTSKNQFFL
human Kabat sgII	P..KG...I.	<b>R.Y.S.STX.N...S</b>	.VT. <u>SV</u> .....S.
human VH FUR1'CL	P..KG...I.	<b>SMFHS.SSY.N...S</b>	.VT. <u>SV</u> .....S.
human Germ-line	P..KG...I.	<b>S.YHS.STY.N...S</b>	.VT. <u>SV</u> .....S.

	<b>Rch 3</b>	<b>CDR 3</b>	<b>Rch 4</b>
7C10 VH mouse	KLNSVTNEDTATYYCAR	<b>YGRVFFDY</b>	WGQGTTLT
human Kabat sgII	..S...AA...V.....	<b>ELPGGYDV</b>	....LV....
human VH FUR1'CL	<u>Q.R...AA...V.....</u>	<b>GRYCSSTSCNWFDP</b>	....LV....
human Germline	..S...AA...V.....		

**FIGURE 23**

	30    CDR 1	48
7C10 VH mouse	DVQLQESGPGLVKPSQSLSTCSVTGYSIT	<u>GGYLWN</u> WIRQFPGNKLEWMG
human germline	Q.....ET.....T.S.....	<u>S</u> S.Y.G .....P..KG... <u>I</u> .
VH Humanized 1	Q.....ET.....T.S.....	.....P..KG.....
VH Humanized 2	Q.....ET.....T.S.....	.....P..KG... <u>I</u> .
VH Humanized 3	Q.....ET.....T.S.....	<u>S</u> .....P..KG... <u>I</u> .
CDR 2                  67    71		
7C10 VH mouse	<u>YISYDGTNNYKPSLKD</u>	RISIT <u>R</u> DTSKNQFFLKLNSVTNEDTATYYCAR
human germline	S.FHS.SSY.N....S	<u>VT.SV</u> .....S...S...AA...V.....
VH Humanized 1	.....	.....T.S.....S...S...AA...V.....
VH Humanized 2	.....	..... <u>VT.S</u> .....S...S...AA...V.....
VH Humanized 3	.....	..... <u>VT.SV</u> .....S...S...AA...V.....
CDR 3		
7C10 VH mouse	<u>YGRVFFDY</u>	WGQGTTLTVSS
human germline	.....	.....LV....
VH Humanized 1	.....	.....LV....
VH Humanized 2	.....	.....LV....
VH Humanized 3	.....	.....LV....

**FIGURE 24**

Mui

GTCAGAACCGCTGCCGCCACCATGAAAGTGGTGGACTCTGTTGACCTCTTGACAGCCATT  
 1 CAGTCTTGCGCACGGCGGTGGTACCTTCACAACACTCAGACAAACATGGAGAACTGTCGGTAA

M	K	V	L	S	L	L	Y	L	L	T	A	I	-
---	---	---	---	---	---	---	---	---	---	---	---	---	---

Leader peptide

CCTGGTATCCTGTCTCAGGTGCAGCCTCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCG  
 61 GGACCATAGGACAGAGTCCACGTCGAAGTCCTCAGCCCCGGTCCTGACCACCTCGGAAGC

P	G	I	L	S	Q	V	Q	L	Q	E	S	G	P	G	L	V	K	P	S	-
---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---

GAGACCCTGTCCCTCACCTGCACTGTCTGGTTACTCCATCACCGGTGGTTATTTATGG  
 121 CTCTGGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTGGCCACCAATAATACC

30	<i>CDR 1</i>													180						
E	T	L	S	L	T	C	T	V	S	G	Y	S	I	<u>T</u>	<u>G</u>	<u>G</u>	<u>Y</u>	<u>L</u>	<u>W</u>	-

AACTGGATACGGCAGCCCCCAGGGAAAGGGACTGGAGTGGATGGGTATATCAGCTACGAC  
 181 TTGACCTATGCCGTGGGGTCCCTCCCTGACCTCACCTACCCCATAAGTCGATGCTG

48	<i>CDR 2</i>													240						
N	W	I	R	Q	P	P	G	K	G	L	E	W	<u>M</u>	G	<u>Y</u>	<u>I</u>	<u>S</u>	<u>Y</u>	D	-

KpnI

GGTACCAATAACTACAAACCCTCCCTCAAGGATCGAACATCACCATATCACGTGACACGTCC  
 241 CCATGGTTATTGATGTTGGGAGGGAGTCCCTAGCTTAGTGGTATAGTGCAGTGTGAGG

67	<i>CDR 3</i>													300						
G	T	N	N	Y	K	P	S	L	K	D	R	<u>I</u>	T	I	S	<u>R</u>	D	T	S	-

AAGAACCAAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGGACACTGCAGTGTATTAC  
 301 TTCTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCTGTGACGTACATAATG

71	<i>BamHI</i>													360						
K	N	Q	F	S	L	K	L	S	S	V	T	A	A	D	T	A	V	Y	Y	-

TGTGCGAGATACTGGTAGGGTCTCTTTGACTACTGGGCCAGGGAACCTGGTCACCGTC  
 361 ACACGCTCTATGCCATCCCAGAAGAAACTGATGACCCGGTCCCTGGGACCAAGTGGCAG

420	<i>CDR 3</i>													420						
C	A	R	<u>Y</u>	G	R	V	F	F	D	Y	W	G	Q	G	T	L	V	T	V	-

BamHI

TCCTCAGGTGAGTGGATCCTCTGCG  
 421 AGGAGTCCACTCACCTAGGAGACGC

445	<i>BamHI</i>													445		
S	S	-														-

## FIGURE 25

MluI

GTCAGAACGCGTGCCGCCACCATGAAAGTGTTGAGTCTGTTGTACCTCTTGACAGCCATT  
 1 -----+-----+-----+-----+-----+-----+ 60  
 CAGTCTGCGCACGGCGGTGGTACTTCACAACTCAGACAAACATGGAGAACTGTCGGTAA

M K V L S L L Y L L T A I -  
 Leader peptide

CCTGGTATCCTGCTCAGGTGCAGCTTCAGGAGTCGGGCCAGGACTGGTGAAGCCTCG  
 61 -----+-----+-----+-----+-----+-----+ 120  
 GGACCATAGGACAGAGTCCACGTCGAAGTCCTCAGCCCAGGTGACCAACTTCGGAAGC

P G I L S Q V Q L Q E S G P G L V K P S -  
 Leader peptide

GAGACCTGTCCTCACCTGCACTGTCTGGTTACTCCATCACGGTGGTTATTATGG  
 121 -----+-----+-----+-----+-----+-----+ 180  
 CTCTGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTCGCCACCAATAATACC  
 30    CDR 1  
E T L S L T C T V S G Y S I T G G Y L W -  
 Leader peptide

AACTGGATAACGGCAGCCCCAGGAAGGGACTGGAGTGGATCGGGTATATCAGCTACGAC  
 181 -----+-----+-----+-----+-----+-----+ 240  
 TTGACCTATGCCGTGGGGTCCCTCCCTGACCTCACCTAGCCCATAAGTCGATGCTG  
 48  
N W I R Q P P G K G L E W I G Y I S Y D -  
 Leader peptide

KpnI

GGTACCAATAACTACAAACCTCCCTCAAGGATCGAGTCACCATATCACGTGACACGTCC  
 241 -----+-----+-----+-----+-----+-----+ 300  
 CCATGGTTATTGATGTTGGAGGGAGTCCTAGCTCAGTGGTATAGTGCAGTCAGTCAGG  
 67    CDR 2  
G T N N Y K P S L K D R V T I S R D T S -  
 Leader peptide

AAGAACCAAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACTGCAGTGTATTAC  
 301 -----+-----+-----+-----+-----+-----+ 360  
 TTCTTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCGTGACGTCACATAATG  
 K N Q F S L K L S S V T A A D T A V Y Y -  
 Leader peptide

TGTGCGAGATAACGGTAGGGCTTCTTGTACTACTGGGCCAGGGAACCTGGTCACCGTC  
 361 -----+-----+-----+-----+-----+-----+ 420  
 ACACGCTCTATGCCATCCCAGAAGAAACTGATGACCCGGTCCCTGGGACCAAGTGGCAG  
 71    CDR 3  
C A R Y G R V F F D Y W G Q G T L V T V -  
 Leader peptide

BamHI

TCCTCAGGTGAGTGGATCCTCTGCG  
 421 -----+-----+----- 445  
 AGGAGTCCACTCACCTAGGAGACGC  
 S S -

**FIGURE 26**

MluI

1 GTCAGAACGCGTGCCGCCACCATGAAAGTGTTGAGTCTGTTGTACCTCTTGACAGCCATT  
 1 CAGTCTGCGCACGGCGGTGGTACTTCACAACTCAGACAACTGGAGAACTGTCGGTAA 60

M K V L S L L Y L L T A I -  
 Leader peptide

61 CCTGGTATCCTGTCTCAGGTGCAGCTTCAGGAGTCGGGCCAGGACTGGTGAAGCCTCG  
 61 GGACCATAGGACAGAGTCCACGTCGAAGTCCTCAGCCGGTCCTGACCACCTCGGAAGC 120

P G I L S Q V Q L Q E S G P G L V K P S -

121 GAGACCTGTCCCTCACCTGCACTGTCCTGGTTACTCCATCAGCGTGGTTATTATGG  
 121 CTCTGGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTCGCCACCAATAAATACC  
 30    CDR 1  
 E T L S L T C T V S G Y S I S G G Y L W -  
 AACTGGATAACGGCAGCCCCAGGGAAAGGGACTGGAGTGGATCGGGTATATCAGCTACGAC  
 181 TTGACCTATGCCGTGGGGTCCCTCCCTGACCTCACCTAGCCCATACTCGATGCTG 240

N W I R Q P P G K G L E W I G Y I S Y D -  
 KpnI

241 GGTACCAAACTACAAACCTCCCTCAAGGATCGAGTCACCATATCAGTGGACACGTCC  
 241 CCATGGTTATTGATGTTGGAGGGAGTCCTAGTCAGTGGTATAGTCACCTGTGCAGG  
 67    CDR 2  
 G T N N Y K P S L K D R V T I S V D T S -  
 AAGAACCAAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACTGCAGTGTATTAC  
 301 TTCTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCGTGACGTCACATAATG  
 301 K N Q F S L K L S S V T A A D T A V Y Y -  
 TGTGCGAGATAACGGTAGGGTCTCTTGACTACTGGGCCAGGGAACCTGGTCACCGTC  
 361 ACACGCTCTATGCCATCCCAGAAGAAACTGATGACCCGGTCCCTGGGACAGTGGCAG  
 67    CDR 3  
 C A R Y G R V F F D Y W G Q G T L V T V -  
 BamHI

421 TCCTCAGGTGAGTGGATCCTCTGCG  
 421 AGGAGTCCACTCACCTAGGAGACGC 445

S S

**FIGURE 27**

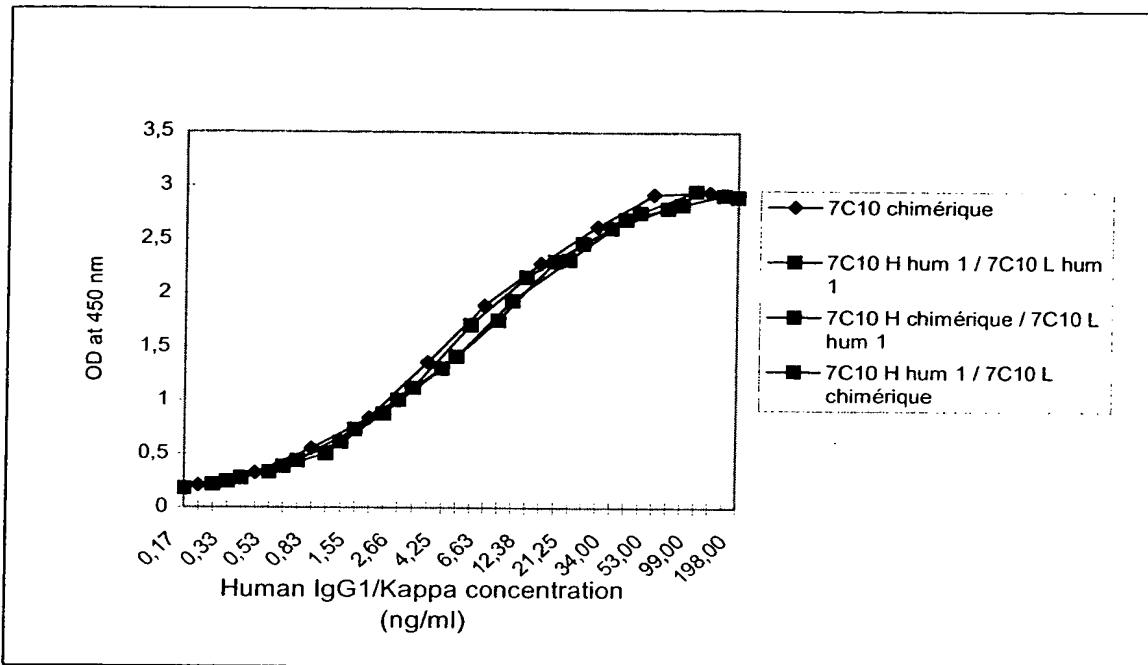


FIGURE 28

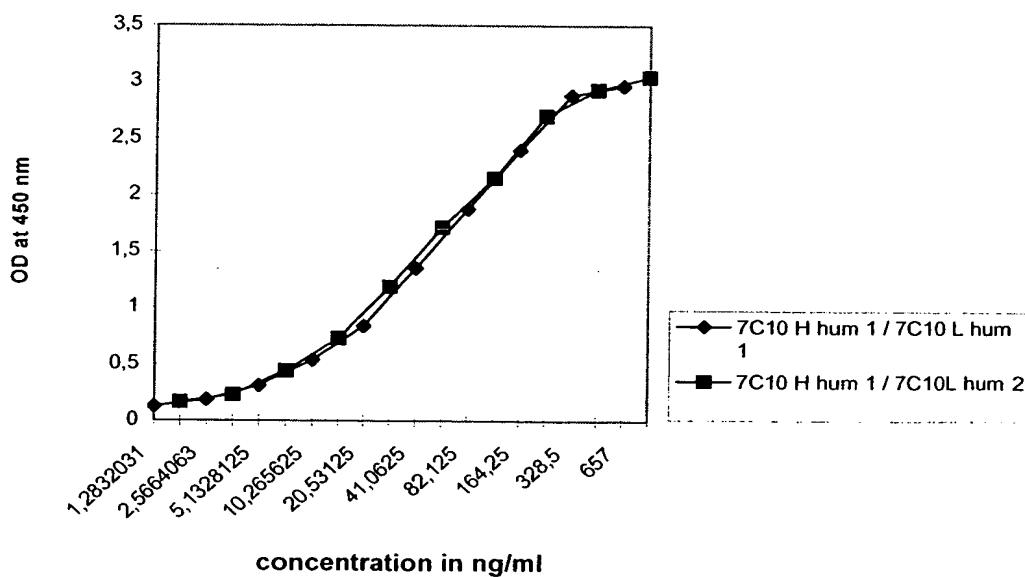


FIGURE 29

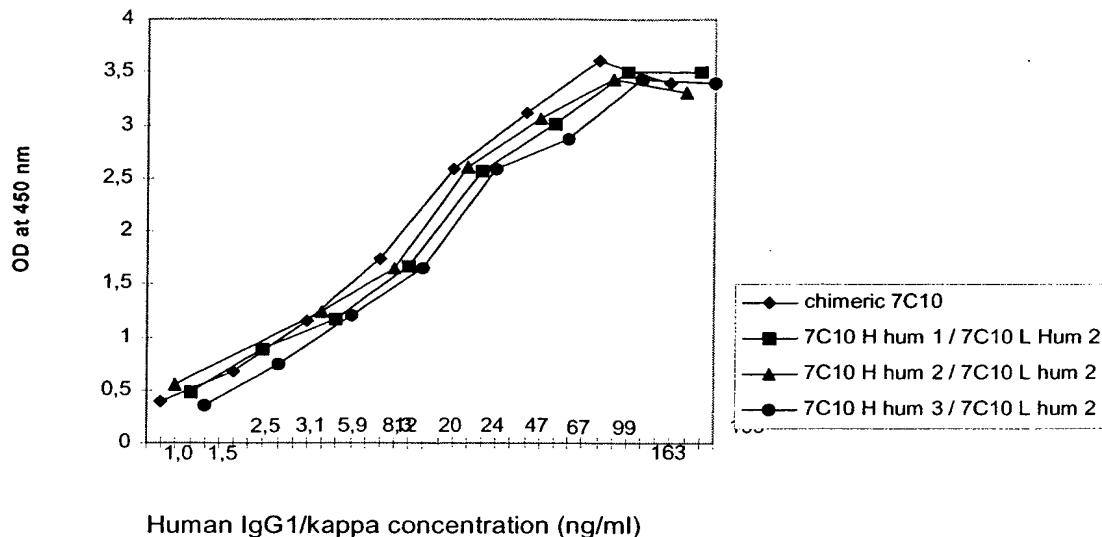


FIGURE 30

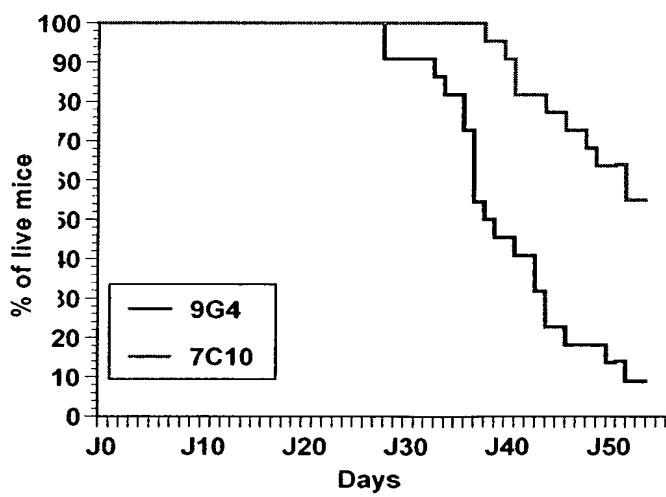
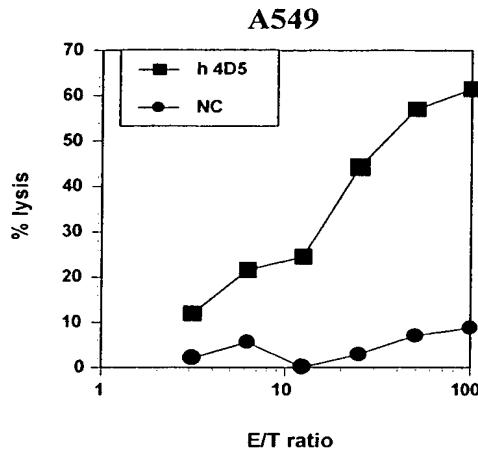
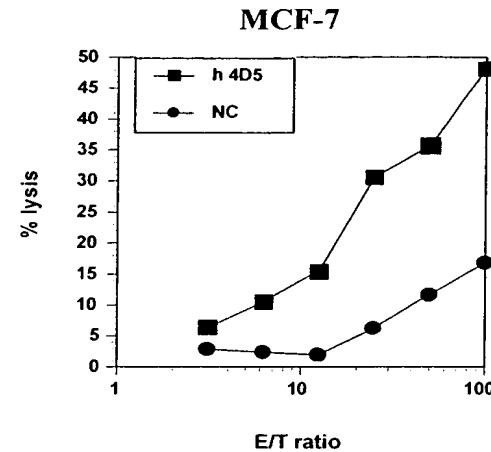


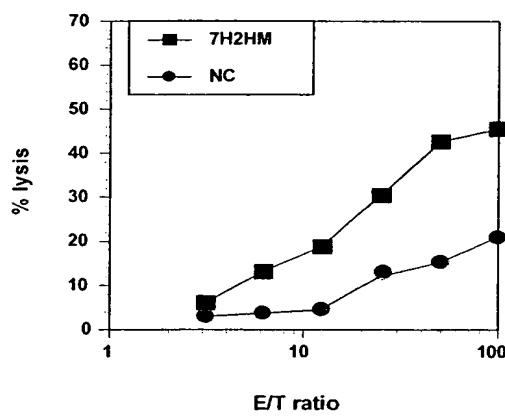
FIGURE 31



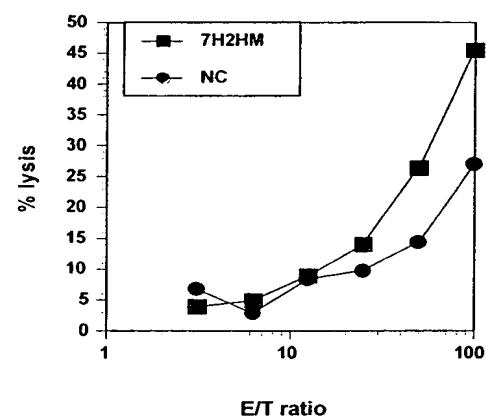
**FIGURE 32A**



**FIGURE 32B**

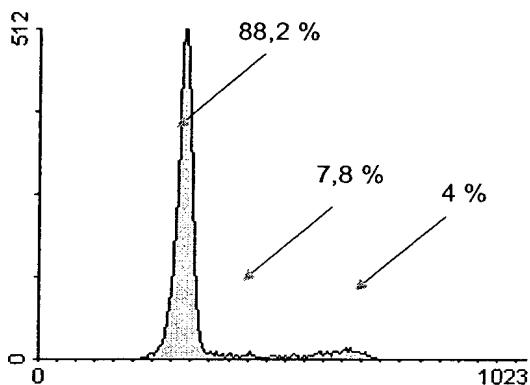


**FIGURE 32C**



**FIGURE 32D**

- IGF1



+ IGF1 (50 ng/ml)

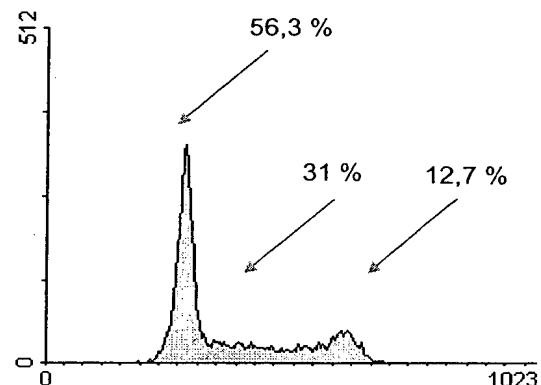


FIGURE 33A

FIGURE 33B

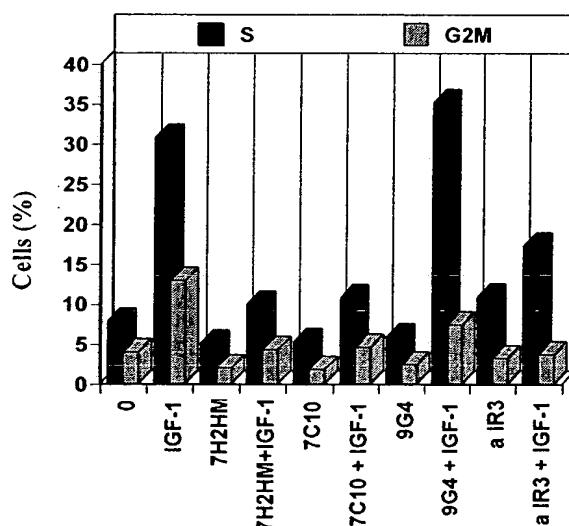


FIGURE 33C

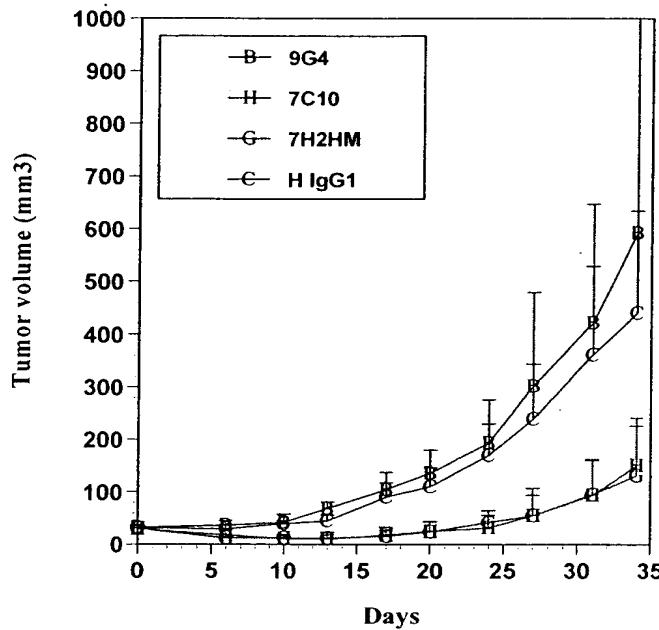


FIGURE 34A

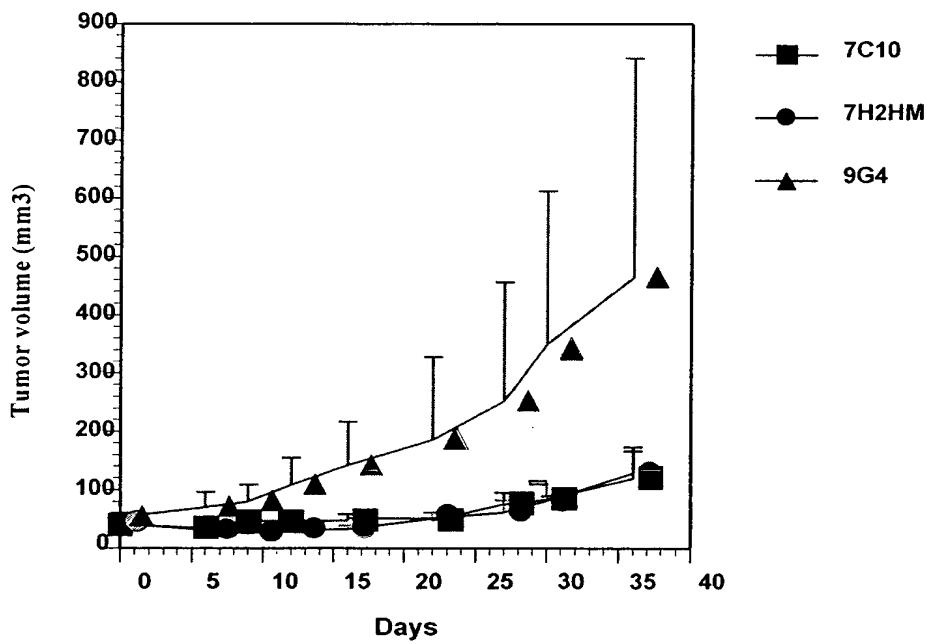
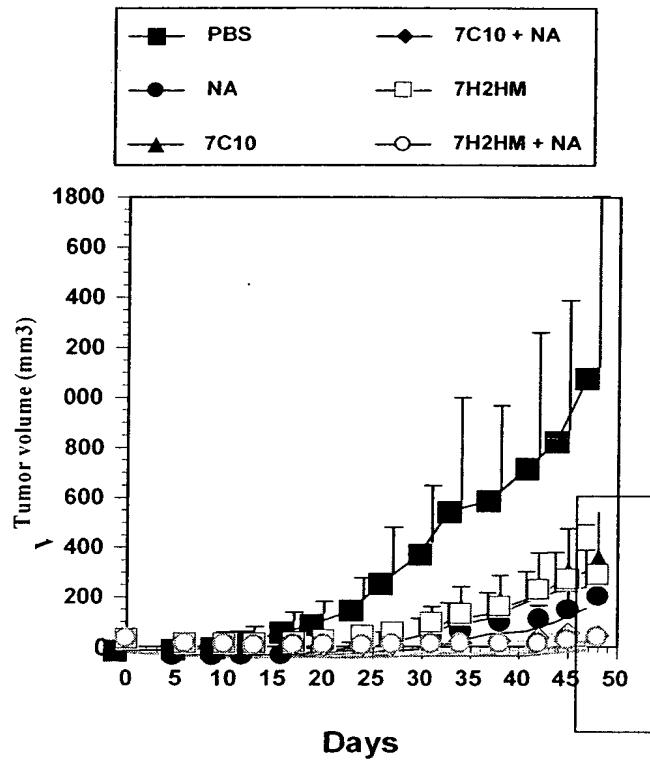
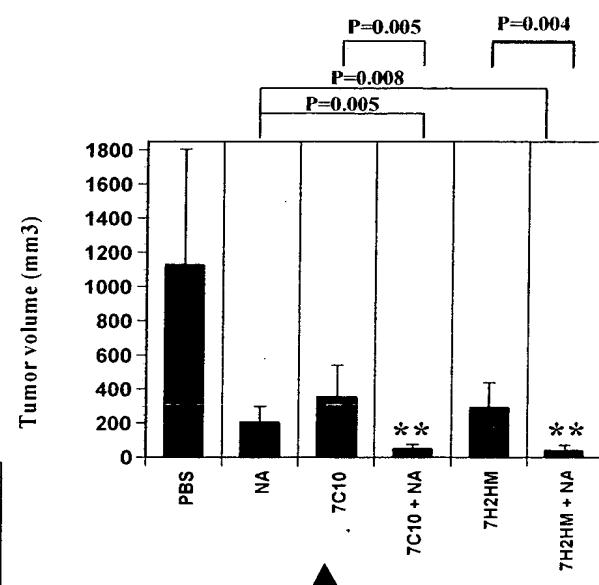


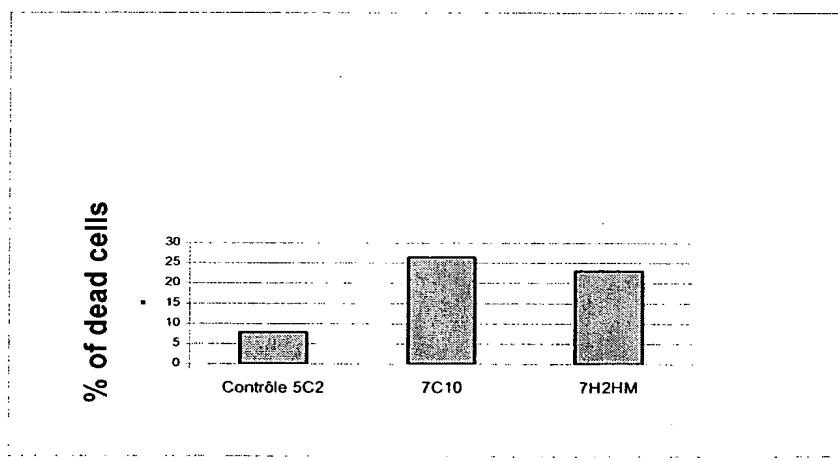
FIGURE 34B



**FIGURE 35A**



**FIGURE 35B**



**FIGURE 36**

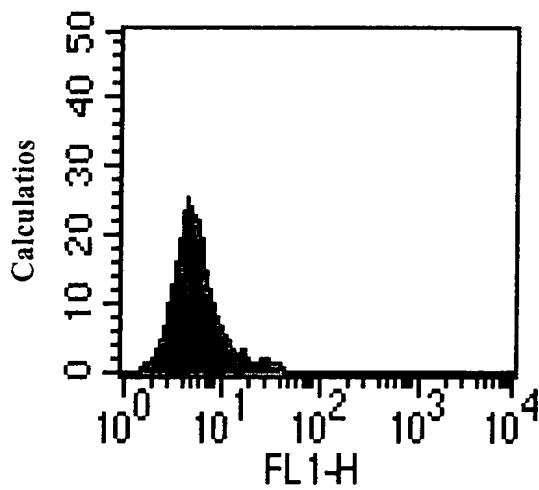


FIGURE 37A

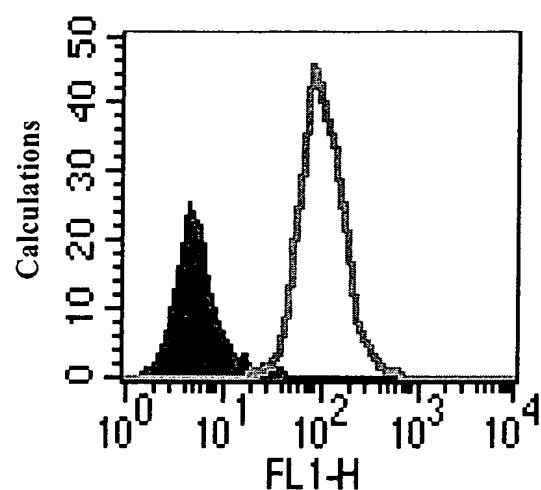


FIGURE 37B

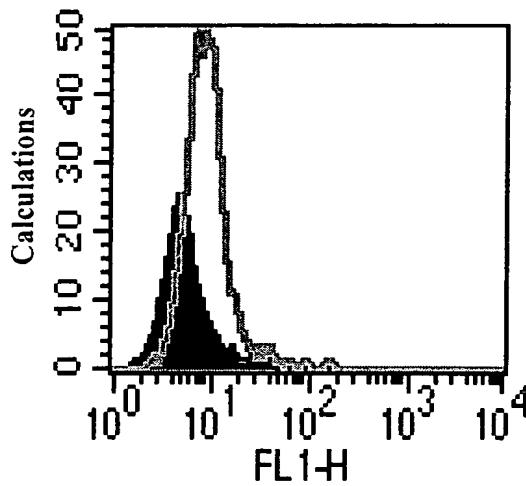


FIGURE 37C

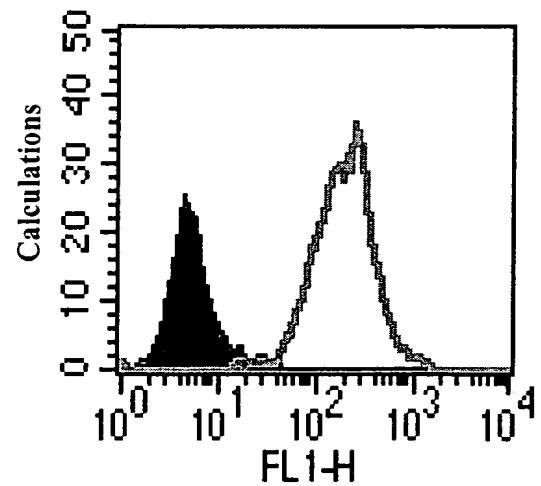


FIGURE 37D

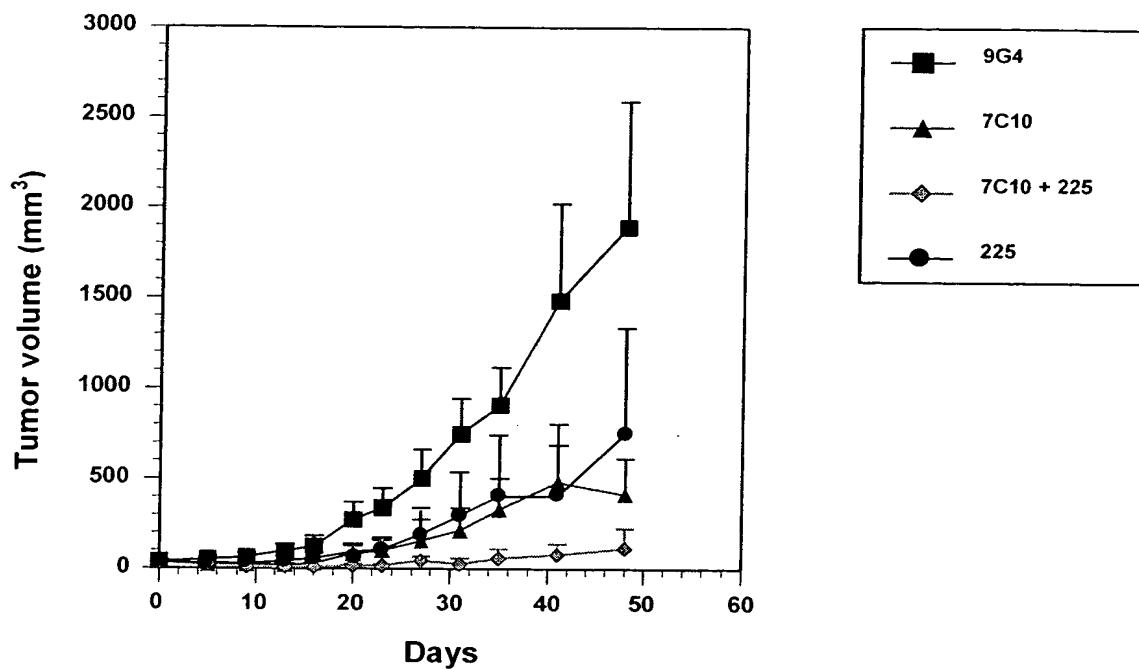


FIGURE 38

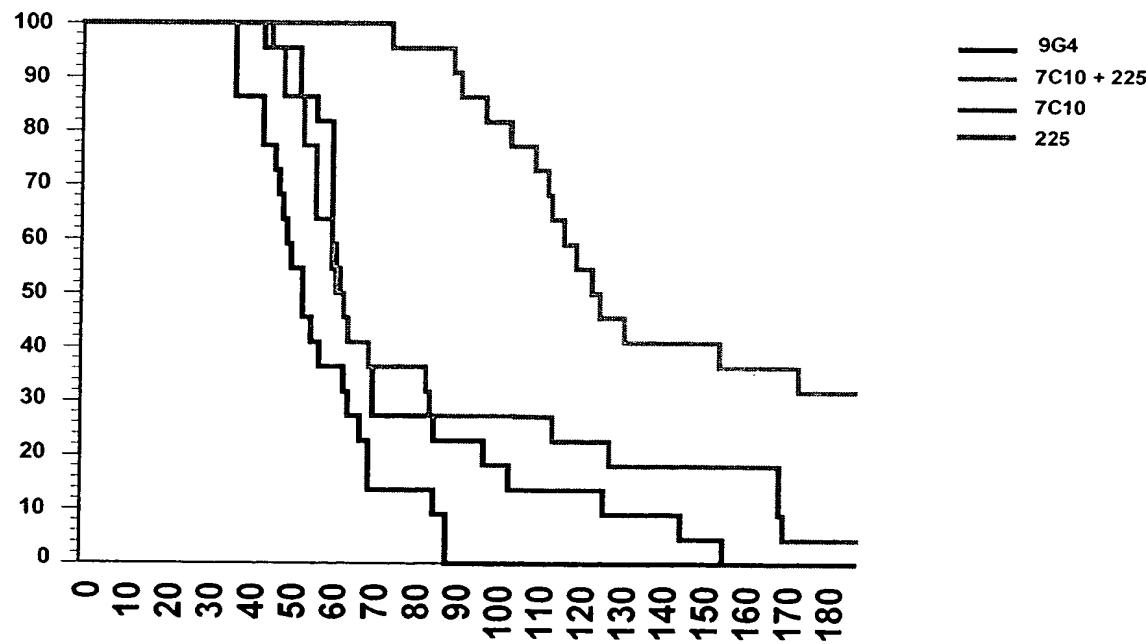


FIGURE 39

FIGURE 40A

IGF-I 50 ng/ml

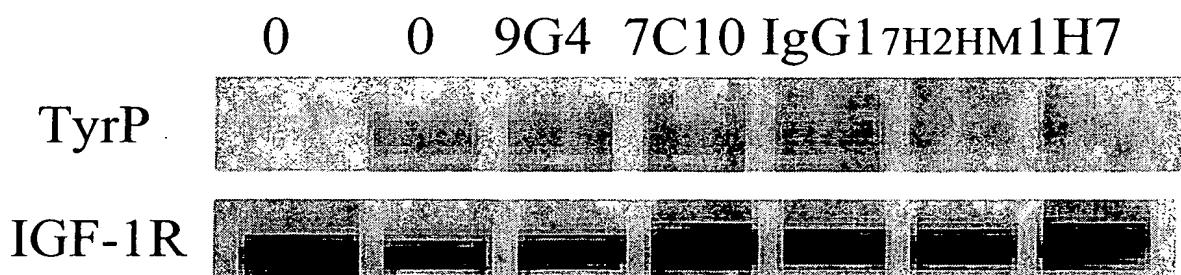


FIGURE 40B

IGF-I 50 ng/ml

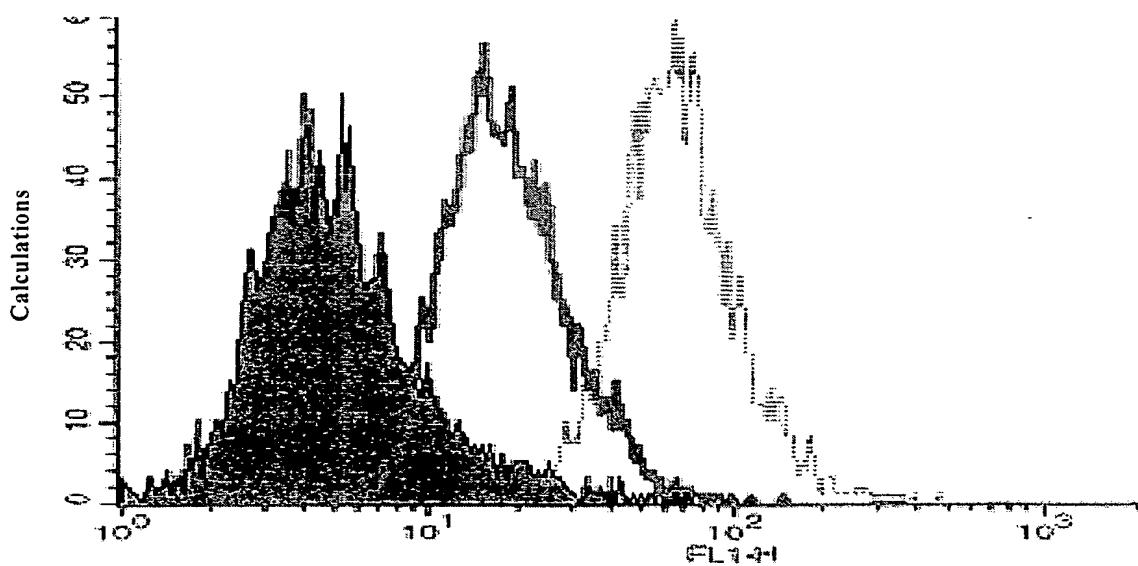
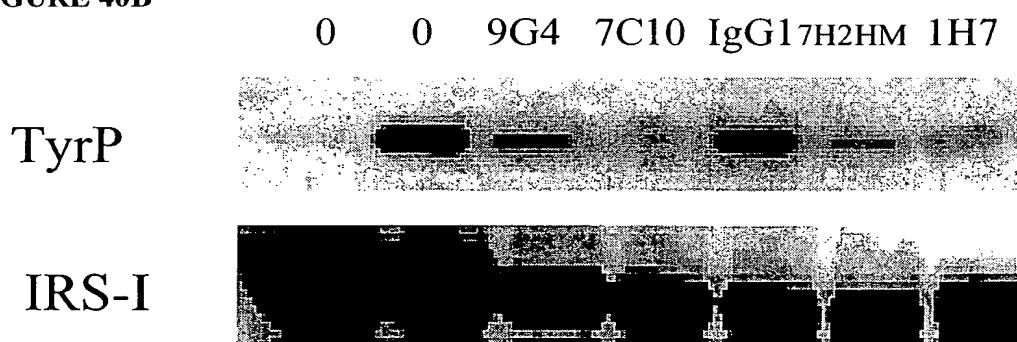
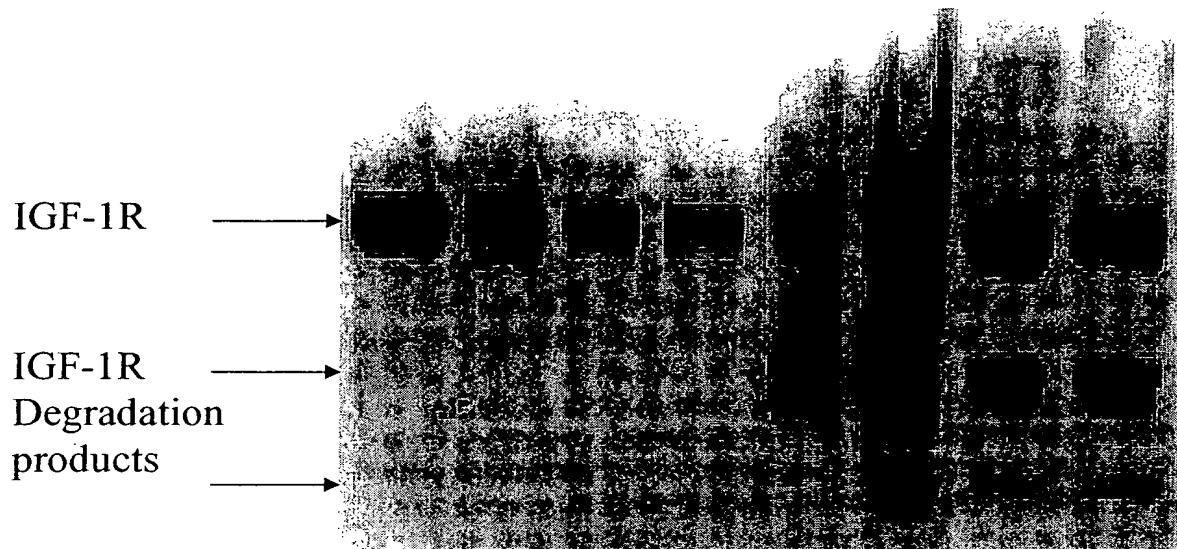


FIGURE 41



Incubation time	5	3	2	1	5	3	2	1
37°C (hours)	9G4 + IGF-I				7C10 + IGF-I			

FIGURE 42A

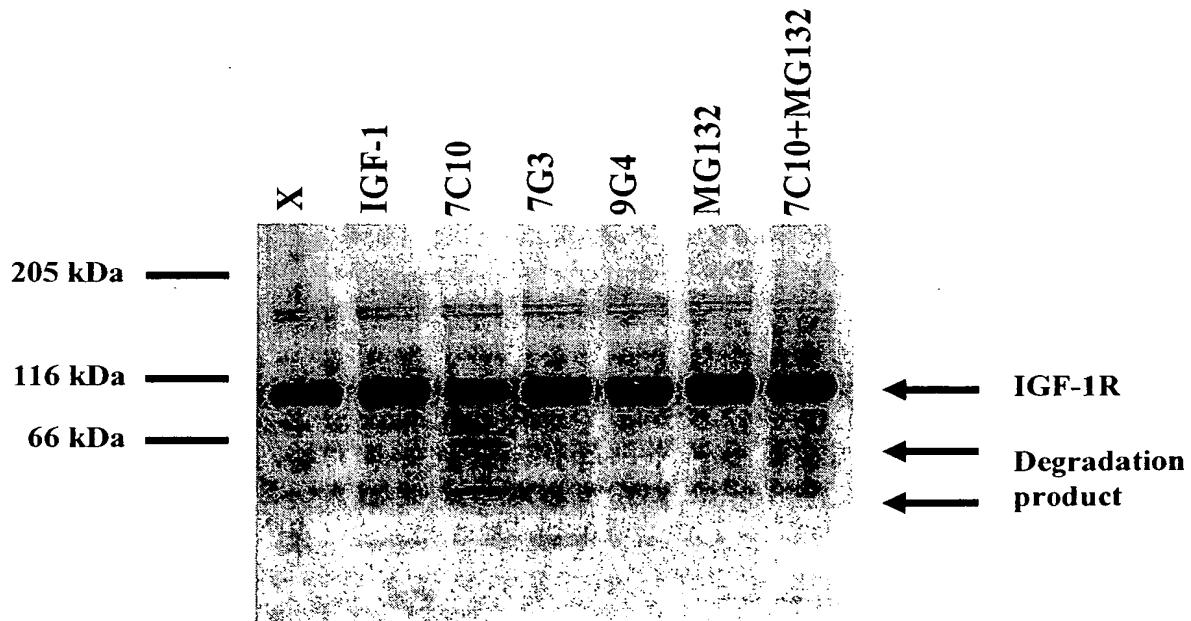
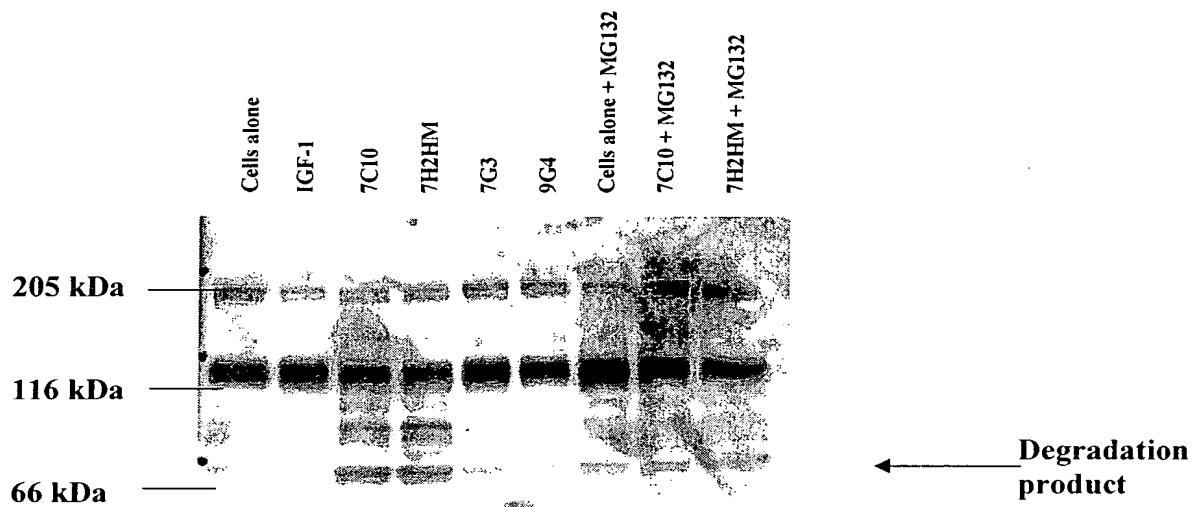
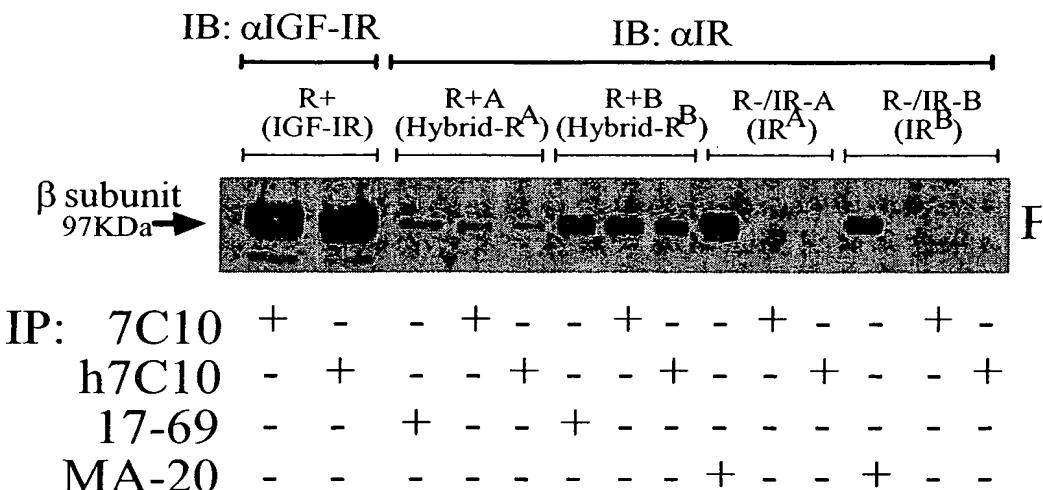


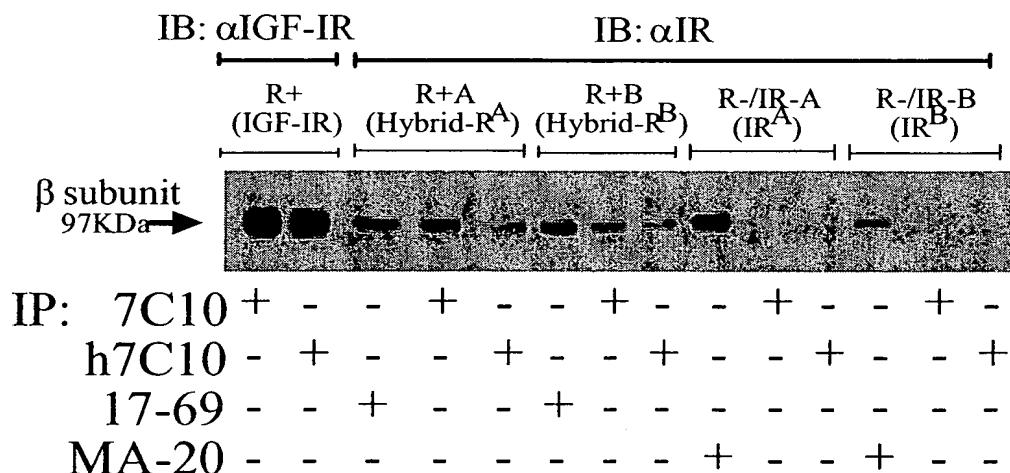
FIGURE 42B



**FIGURE 42C**



**FIGURE 43A**



**FIGURE 43B**

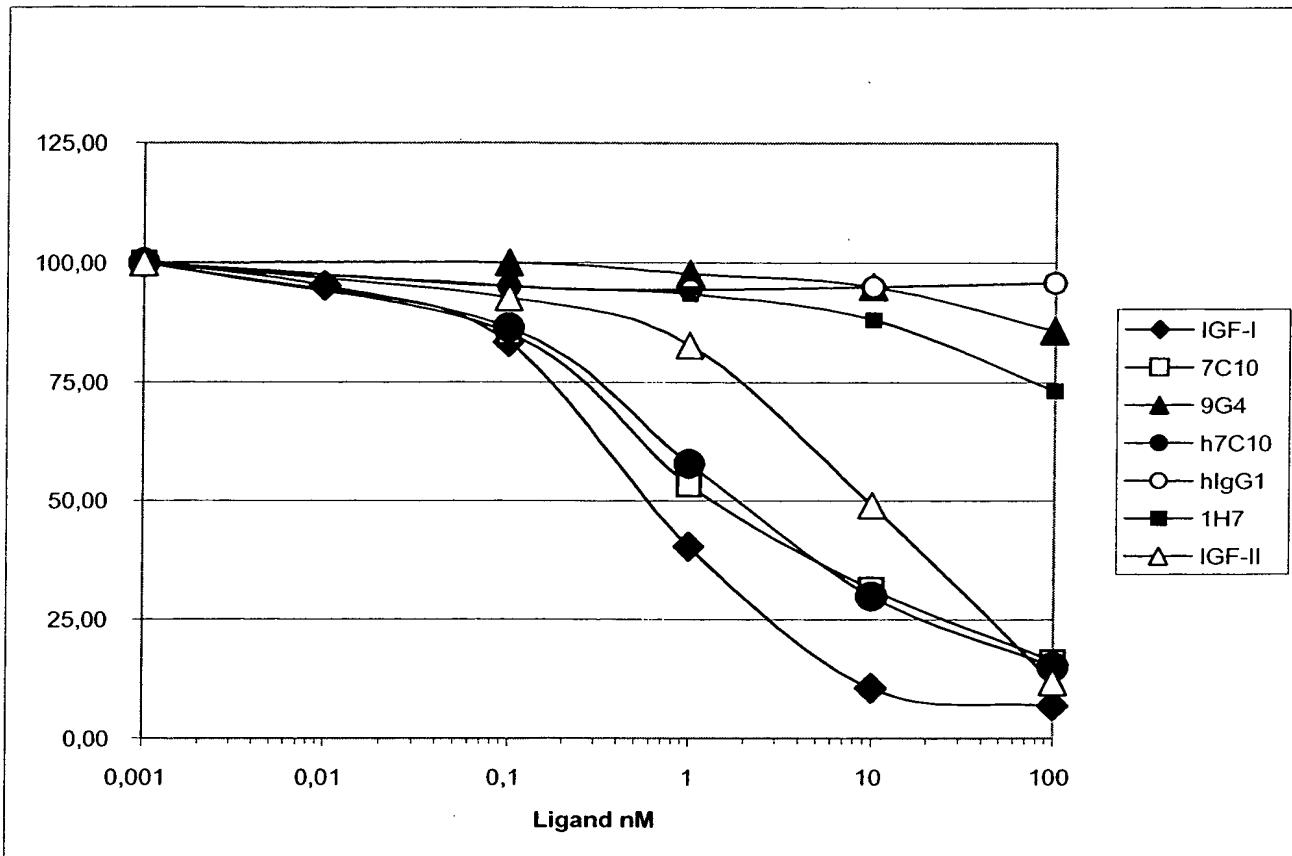


FIGURE 44

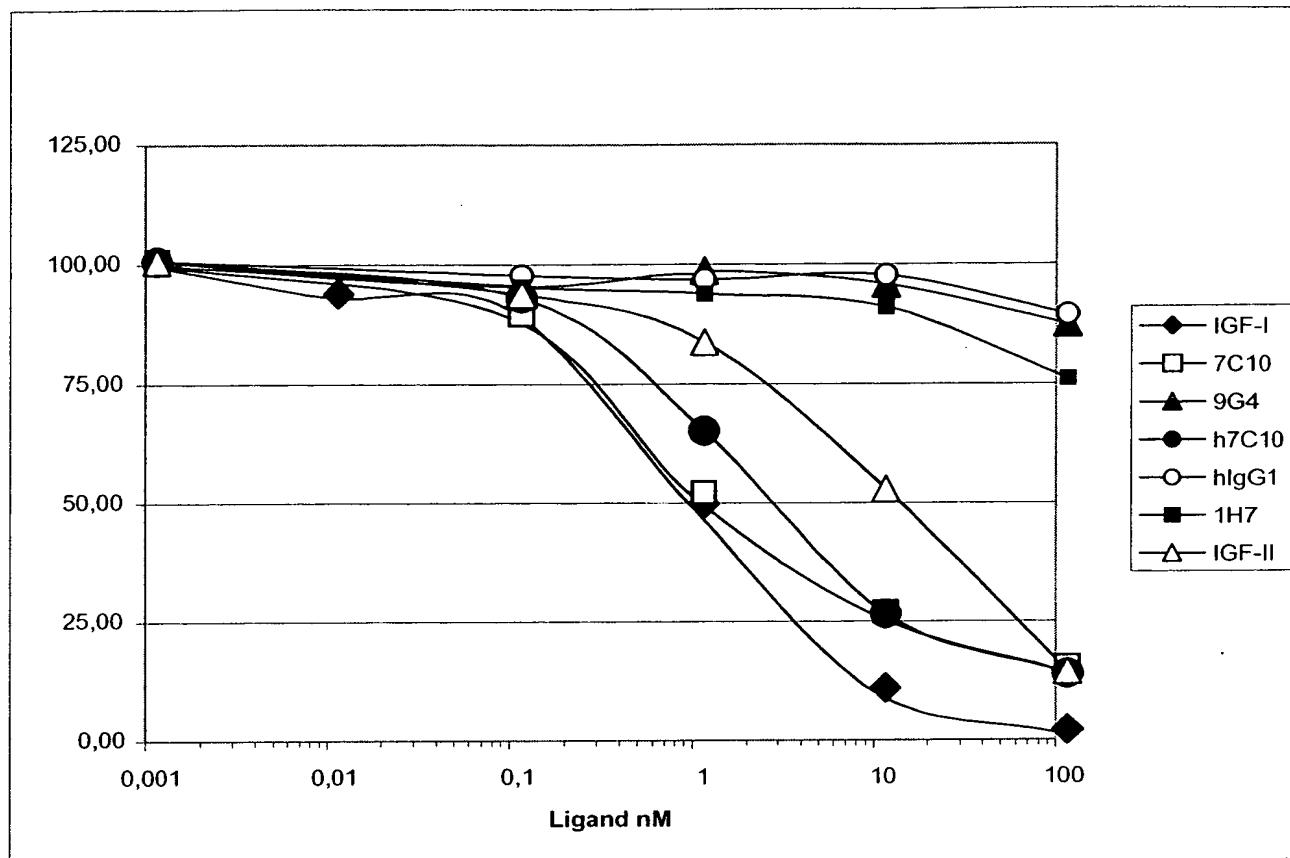


FIGURE 45

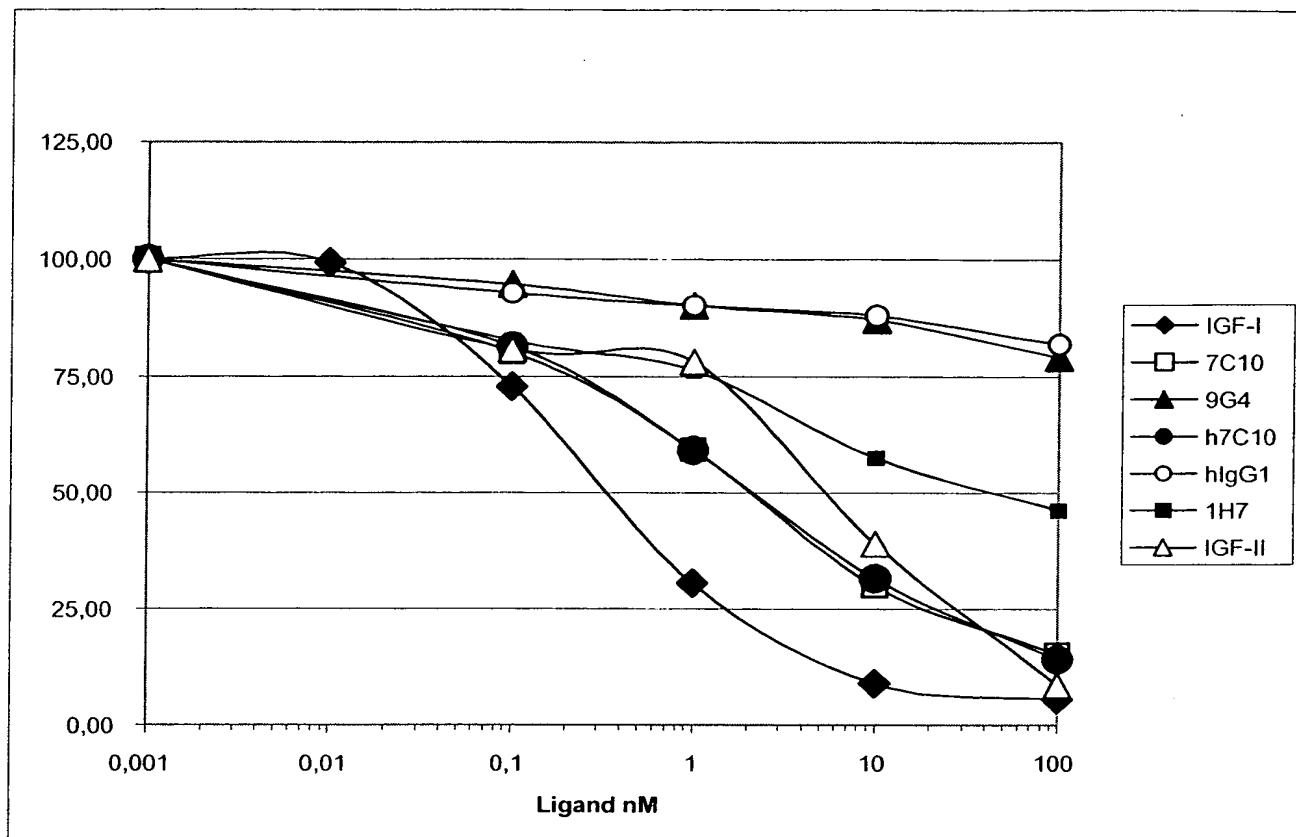
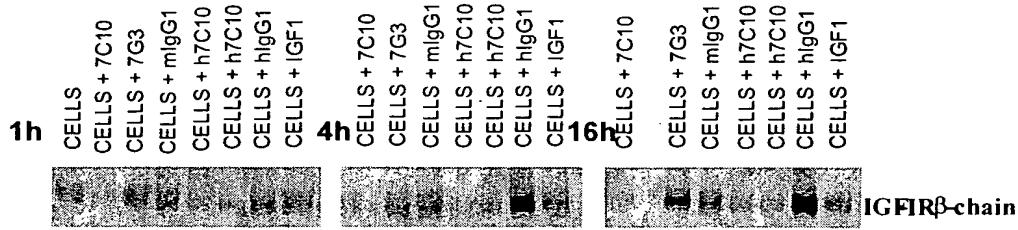
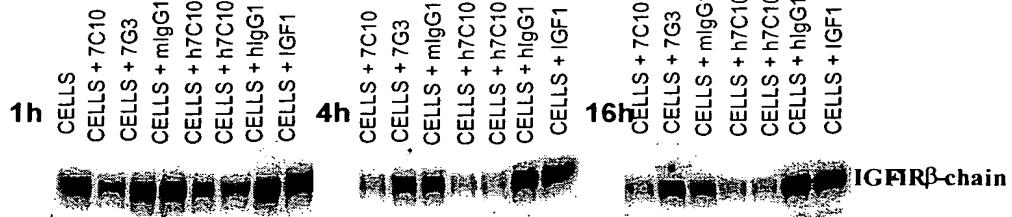


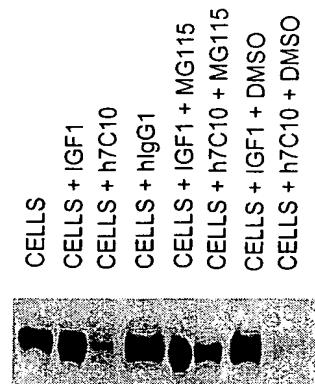
FIGURE 46



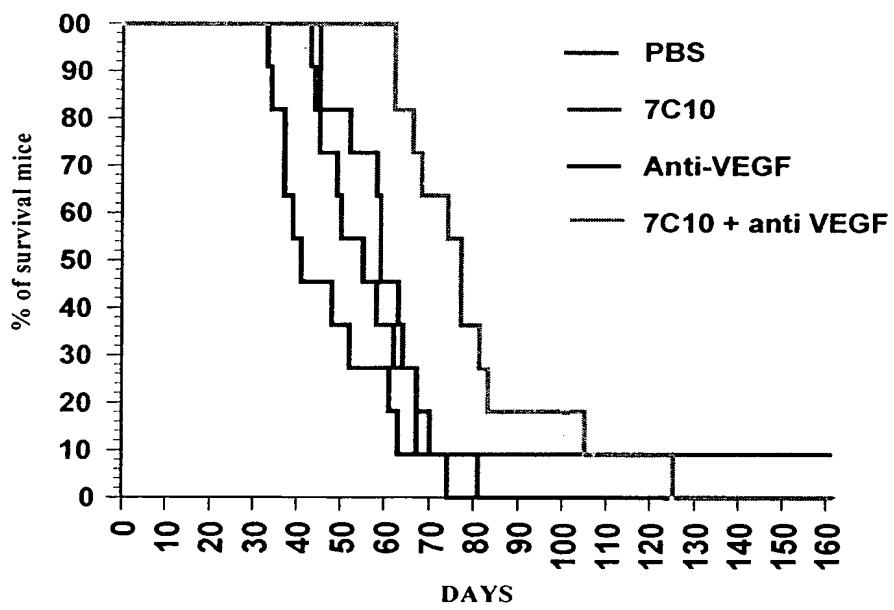
**FIGURE 47A**



**FIGURE 47B**



**FIGURE 48**



**FIGURE 49**

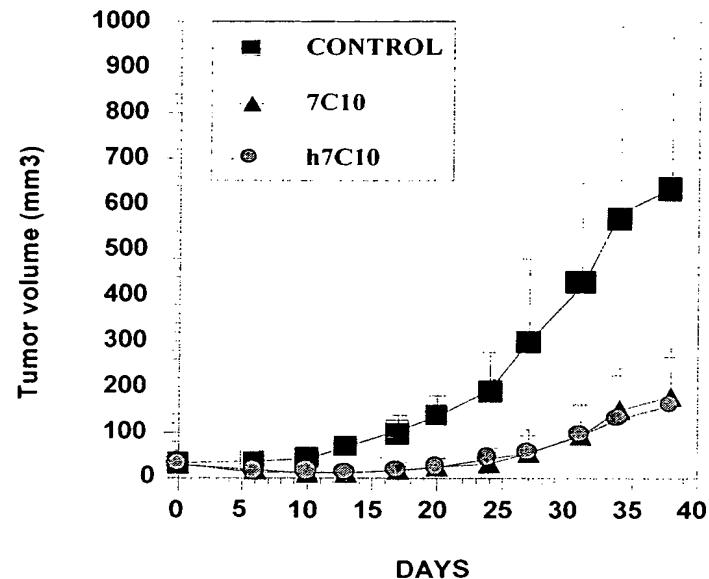


FIGURE 50

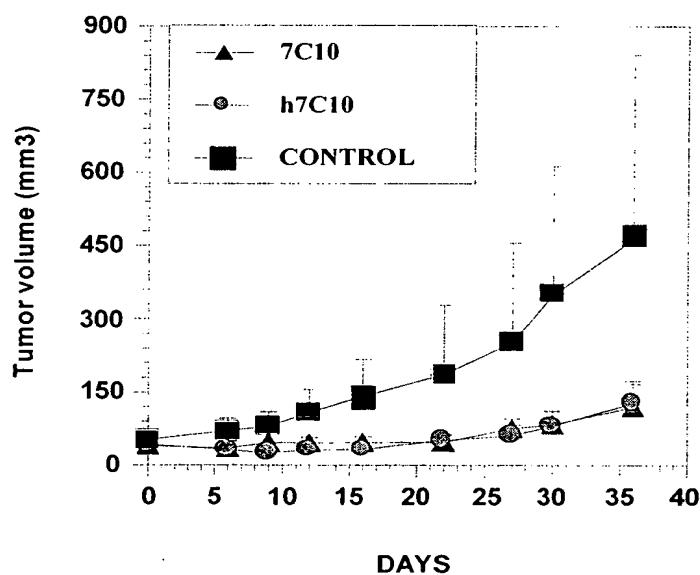
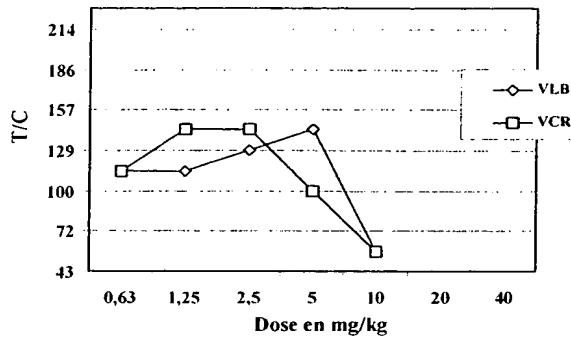
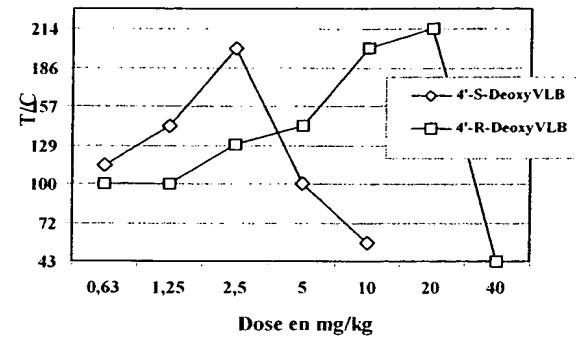


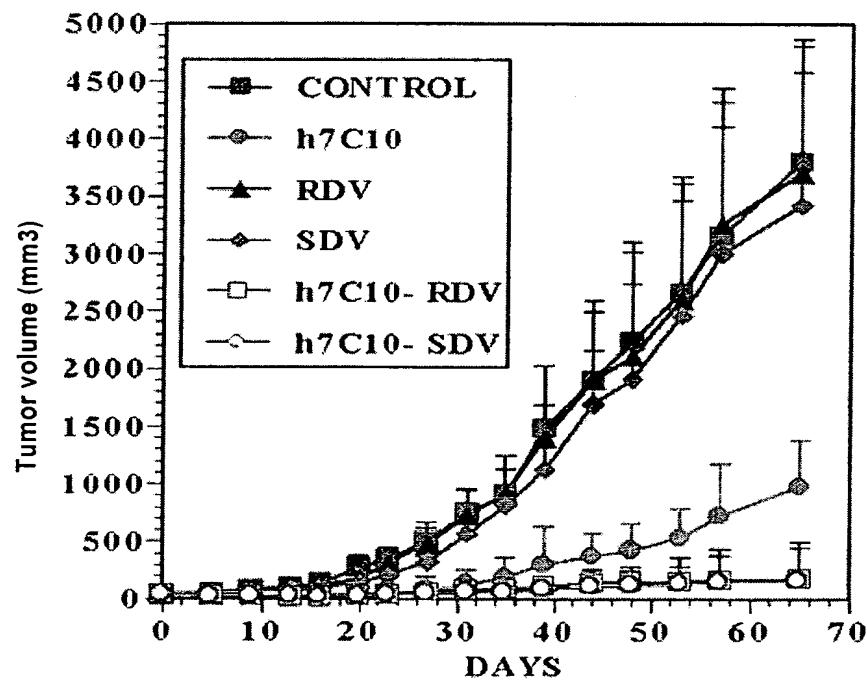
FIGURE 51



**FIGURE 52**



**FIGURE 53**



**FIGURE 54**

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